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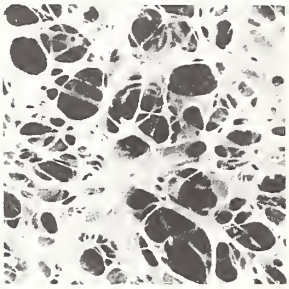

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Research Advances

375 Male Daydreamers...

PROBLEM-SOLVING DOMINATES DAYDREAMING

Daydreaming is a temporary shift of attention away from an ongoing physical or mental task toward a response to some internal stimulus. For children, daydreams serve an important developmental function. But what function does daydreaming serve for adults?

In an attempt to answer this question, Leonard M. Giambra, Ph.D., administered a 344-item psychological questionnaire to 375 adult male daydreamers. This questionnaire was developed previously by psychologists to provide information on the frequency, content, and context of daydreams.

The individuals in the study group, divided into seven age groups ranging from age 17 to 91, were white and the majority were middle or upper-middle class. The youngest group consisted of students from Miami University; the remaining groups were comprised of participants in the Baltimore Longitudinal Aging Study at the Gerontology Research Center of the National Institute of Child Health and Human Development. Dr. Giambra is a senior staff fellow at the Center.

Dr. Giambra's analysis of the responses to the questionnaire reveals the way daydreaming changes throughout life. He reports that the frequency of daydreaming declines with age, with the periods of greatest decline occurring after age 23, after age 44, and after age 74. Additionally, he found that daydreaming reflects current concerns and not suppressed desires.

Most, but not all, people seem to daydream. Young men between the ages of 17 and 23 daydreamed the most in the present study (at least a few times

(more)

daily), possibly reflecting their continued participation in dreary classes or a tendency to become easily bored with whatever they are doing. And, contradicting the popular assumption that older people idle away their time in daydreams, Dr. Giambra found that men over 75 years of age report daydreaming only about once a week, although a quarter of them report the same frequency as the youngest group. As the young become older, the investigator found, daydreaming steadily declined to the low level of the over 75 year old group.

Daydreaming seemed to provide more work than excitement for the men in the study group. Problem solving--such as getting useful clues to a problem or seeing a fresh approach to an old problem--was the most frequent type of activity in the daydreams of every age group except the youngest, where sex had a slight edge. Daydreams about sex and achievement decline steadily with age, Dr. Giambra explains, replaced in the middle age range with an increased level of bizarre-improbable thoughts. This type of daydream decreases in frequency among the very old.

The other categories of daydreams that Dr. Giambra measured--heroic, hostile, fear of failure, and guilt--all appeared relatively infrequently, and they show no major change with age.

For most people, daydreams provide both sight and sound. Ten percent of the men in the present study reported images so vivid that they had difficulty separating daydreams from reality. Furthermore, at least one out of 10 reported "visual images in my daydreams...so vivid I believe they are actually happening." Dr. Giambra points out that an unknown percentage

(more)

of daydreams never were separated from reality by the men, and therefore, were not reported. While visual imagery was consistently high across age categories, accompanying sound as well as daydreams involving only sound occur less frequently with time.

Daydreams offer a flight from the immediate, but Dr. Giambra believes they often do not go far. The present and future showed a nearly equal tendency to be the setting of daydreams for all age groups, and there was no special tendency to linger in the past for anyone. Even men between 75 and 91, who have the highest frequency of daydreams about the past, showed an almost equal tendency to daydream about the present and future.

Men age 24 to 34 were least likely to daydream about the past, perhaps because this part of a man's life is a particularly busy one, with heavy demands from both family and job. His strongest concerns are with the present, therefore, rather than the past or future.

Men in this age group are unique in other aspects of daydreaming, as well. Compared to the 17- to 23-year-olds, they show a sharp decrease in the frequency of daydreaming and in visual and auditory imagery, all of which increase again among men in the next age category (35 to 44). In four of the eight types of daydream content, the 24 to 34 age group also drops sharply below those of the youngest men. These men are daydreaming less, but there is little evidence that they are "enjoying it more", Dr. Giambra explains; the only category of daydreams they experience more frequently than younger men is problem solving.

Daydreaming intrudes uninvited on the daydreamer, often without (and

(more)

probably beyond) conscious control. All age groups except the oldest report that at least 10 percent of their daydreams occur when they are not paying attention to an immediate task.

According to Dr. Giambra, scientists have known little until now about the actual content of these intruding daydreams, and even less about their meaning. The Freudian interpretation holds that daydreams are repressed desires, consisting of a "kaleidoscope of thoughts about sex and hostility that result in feelings of guilt." However, Dr. Giambra believes that it is clear from the present data that daydreams reflect the current concerns, interests, and problems of the individuals. Daydreams, therefore, act as an alternate channel in which information can be organized and reorganized creatively. The fact that problem solving heads the list of daydream types supports this interpretation, and the fact that guilt is the least frequent type of daydream across all age categories makes the Freudian analysis seem most unlikely to Dr. Giambra.

The investigator published a report of his findings in the *International Journal of Aging and Human Development*, 2, 1974; and in *Psychology Today*, December 1974.

#

Research Advances

SEATTLE SCIENTISTS WORK TOWARD BIOLOGICAL CONTROL OF MOSQUITOES

The discovery of a previously unknown phase in the life cycle of a parasite fatal to mosquitoes opens exciting possibilities in the biological control of these disease carriers. Although investigators have known for many years that a particular parasitic water mold is fatal to mosquito larvae under natural conditions, it has never been possible to produce the same result in the laboratory. Consequently, scientists have been unable to make deliberate use of the water mold in areas where mosquito control is vital.

Howard C. Whisler, Ph.D., and Stephen L. Zebold, of the University of Washington, report that an intermediate host is necessary in the life cycle of the infective fungus, *Coelomomyces psorophorae*. This knowledge has enabled the investigators to infect the larvae of the mosquito *Culiseta inornata* under relatively simple laboratory conditions. They found that the spores (or seeds) of the Coelomomyces require two different hosts: first, a copepod (a minute marine animal) called *Cyclops vernalis*, and second, the mosquito larvae. Spores from the mosquito larvae then infect more copepods. Thus, the hosts must alternate for the spores to grow. This alternation of hosts, called heteroecism, is common in some other fungi, but has not been noted previously in the large class of algae-like fungi called *Phycomycetes*, to which the Coelomomyces belong.

Dr. Whisler and Zebold, whose work is funded by the National Institute of Allergy and Infectious Diseases, are now investigating other species of *Coelomomyces*. They are also seeking ways of using this information for the biological control of large populations of mosquitoes, including those that

(more)

Mosquitoes (Cont'd)

carry the organisms causing malaria and yellow fever. Although the mosquito used in this study, *Culiseta inornata,* has not been identified as a disease carrier, its close relative *Culiseta melanura* does carry the Eastern equine encephalitis virus, which causes sometimes fatal encephalitis in humans, as well as in horses and wild birds.

Over the years, many different strains of *Coelomomyces* have been recognized as natural enemies of different species of mosquitoes. *Coelomomyces* seems to be quite specific for mosquitoes and, therefore, without harmful effects on other insects or on man. When found naturally, the fungus maintains itself in the mosquito environment year after year providing a continuous control on mosquito population growth. However, past attempts to control mosquitoes by introducing *Coelomomyces* into the environment--for instance in the South Seas areas where malaria is a major problem--have been unsucessful.

Now that the necessity for an intermediate host has been recognized, the possibilities for biological control of mosquitoes are considerably improved. Dr. Whisler and Zebold hope that introduction of the copepod as well as the *Coelomomyces* to an experimental situation will enable the fungus to follow its normal life cycle and to infect mosquitoes as it does under natural conditions. This method of biological control may thus diminish populations of disease-carrying mosquitoes without the use of chemical insecticides.

Dr. Whisler and Zebold reported their findings in the October 25 issue of *Nature*.

#

Research Advances

WEGENER'S GRANULOMATOSIS IS TREATED WITH CYTOTOXIC DRUGS

Good results in treating patients with a rare but once universally-fatal disease called Wegener's granulomatosis, have been reported by scientists at the National Institute of Allergy and Infectious Diseases (NIAID).

Sheldon M. Wolff, M.D., NIAID clinical director, was moderator of a panel of Institute scientists who recently discussed their treatment and study during the past 13 years of 21 victims of this disease. The panel included Anthony S. Fauci, M.D., David C. Dale, M.D., and Robert G. Horn, M.D. (Dr. Dale is now at the University of Washington and Dr. Horn is at Vanderbilt University.)

Wegener's granulomatosis was defined as a distinct clinical entity in 1936. It is characterized by granuloma formation and inflammation of small blood vessels, particularly in the upper respiratory tract, the lungs, and the kidneys. Although the cause remains unknown, investigators believe it is the result of a hypersensitivity or allergic reaction to an as yet unidentified allergen.

The disease affects more males than females, and the age distribution of patients ranges from three months to 75 years. It generally begins with severe upper respiratory symptoms. Pulmonary symptoms are also common, but, as the disease progresses, any organ system of the body can become involved. If untreated, more than 90 percent of the patients die within two years, usually from kidney disease. The mean survival time is five months.

Many treatments have been tried over the years. Adrenal corticosteroids were thought to be beneficial, but they rarely prolonged life. Antibiotics

(more)

are sometimes useful in preventing secondary infections, but they do not affect the underlying disease. In the mid 1960s, physicians began using drugs that kill cells and suppress the body's immune response (known as cytotoxic immunosuppressive drugs). NIAID scientists now report that their use of these drugs, particularly one called cyclophosphamide, has resulted in long-lasting remissions, often of many years duration.

Early diagnosis is difficult but important. There is no specific laboratory test or clinical feature that readily identifies Wegener's granulomatosis. However, the long-term studies at the NIH Clinical Center have enabled investigators to assemble a list of characteristic clinical and pathological findings to help physicians diagnose this disease more precisely.

Biopsy of kidney tissue is one of the most important tools in diagnosis and in assessing the extent of kidney involvement. If treatment can begin before irreversible damage is done, the patient's chance of survival is obviously much greater. Often biopsy will show early involvement even when kidney function is entirely normal and the granulomatosis is considered to be a localized pulmonary condition. In the Clinical Center study, follow-up biopsies, performed from four months to five years after treatment began, showed healed lesions and no evidence of active disease.

Response to cytotoxic drugs is very good. Of the 21 patients treated at the Clinical Center, 15 patients are in remission including one for nearly seven years. Six of these are no longer receiving medication. Of the other six patients, one had a remission but died of an unrelated cause, three died before an adequate course of the drug could be given, and two died of their

(more)

Wegener's Granulomatosis (Cont'd)

disease. Since cytotoxic therapy can produce adverse side effects, dosage must be carefully monitored and constantly adjusted. Although the appropriate duration of treatment is uncertain, the panel believes that tapering off and even discontinuing treatment should be attempted if the patient has been free of all traces of the disease for one year.

This discussion was presented at a Combined Clinical Staff Conference at NIH. An edited transcript was published in the *Annals of Internal Medicine*, October, 1974.

#

INCREASED WILLINGNESS--Women who are free of any cancer symptoms seem to be increasingly willing to participate in annual checkups for cancer, reports the National Cancer Institute. This fact will make screening programs for cancers of the breast and cervix more effective in reaching their goal of obtaining the earliest possible detection in the largest number of people.

KIDNEY CANCER--Wilms' tumor is a rare cancer of the kidney that usually occurs in early childhood. Scientists at the National Cancer Institute believe that Wilms' tumor is the consequence of an abnormality in the developing embryo.

Photo Feature

SCIENTISTS LINK EMPHYSEMA TO GENETIC ENZYME DEFECT

Emphysema, the most rapidly increasing cause of death in the United States, is now the third leading cause of death from respiratory disease. Emphysema takes many forms. One type has recently been attributed to a genetic enzyme defect known as alpha-l-antitrypsin deficiency.

Early detection and treatment can do much to prevent some consequences of this enzyme deficiency, which may be responsible for as much as one-third of the emphysema in the United States today. A screening test for alpha-l-antitrypsin deficiency has been developed which is now being performed on a number of population groups to identify persons who are affected but who have not yet developed emphysema, in order to improve the quality of life and maybe for genetic counseling. At the same time, scientists are searching for the underlying genetic defect as well as possible methods for prevention of the associated emphysema.

When inherited from both parents, alpha--l-antitrypsin deficiency has been shown to be associated with the development of a severe form of familial emphysema which attacks young adults. This emphysema is rapidly progressive, resulting in death by the early 40's. It has not yet been determined whether individuals with only one gene for the defect are also at higher risk, but early results indicate that at least one group of such carriers may be at particularly high risk.

(more)

Emphysema (Cont'd)

Emphysema and chronic bronchitis, when considered together, are referred to as chronic obstructive pulmonary disease. Both emphysema and chronic bronchitis produce breathlessness, cough, and increased susceptibility to respiratory failure and death. Chronic obstructive pulmonary disease attacks middle-aged men and women and is particularly common in smokers. It is now believed that early abnormalities (physiologic and biochemical) related to emphysema and chronic bronchitis may be detected at a stage when lung damage is still reversible.

A new and promising method has been developed for the early detection of changes in lung function and structure which appear to be the first signs of chronic obstructive pulmonary disease. This method, measurement of closing volume (the amount of air remaining in the lungs after smaller airways collapse at the end of expiration), detects early changes in the lung which are thought to eventually progress to the clinical signs and symptoms of this major health problem. It is presently believed that in persons with abnormal closing volume measurements but with otherwise normal lung function tests, the progression of disease may be reversed and disability prevented with proper treatment and the cessation of smoking.

The National Heart and Lung Institute considers this to be an important area of study.

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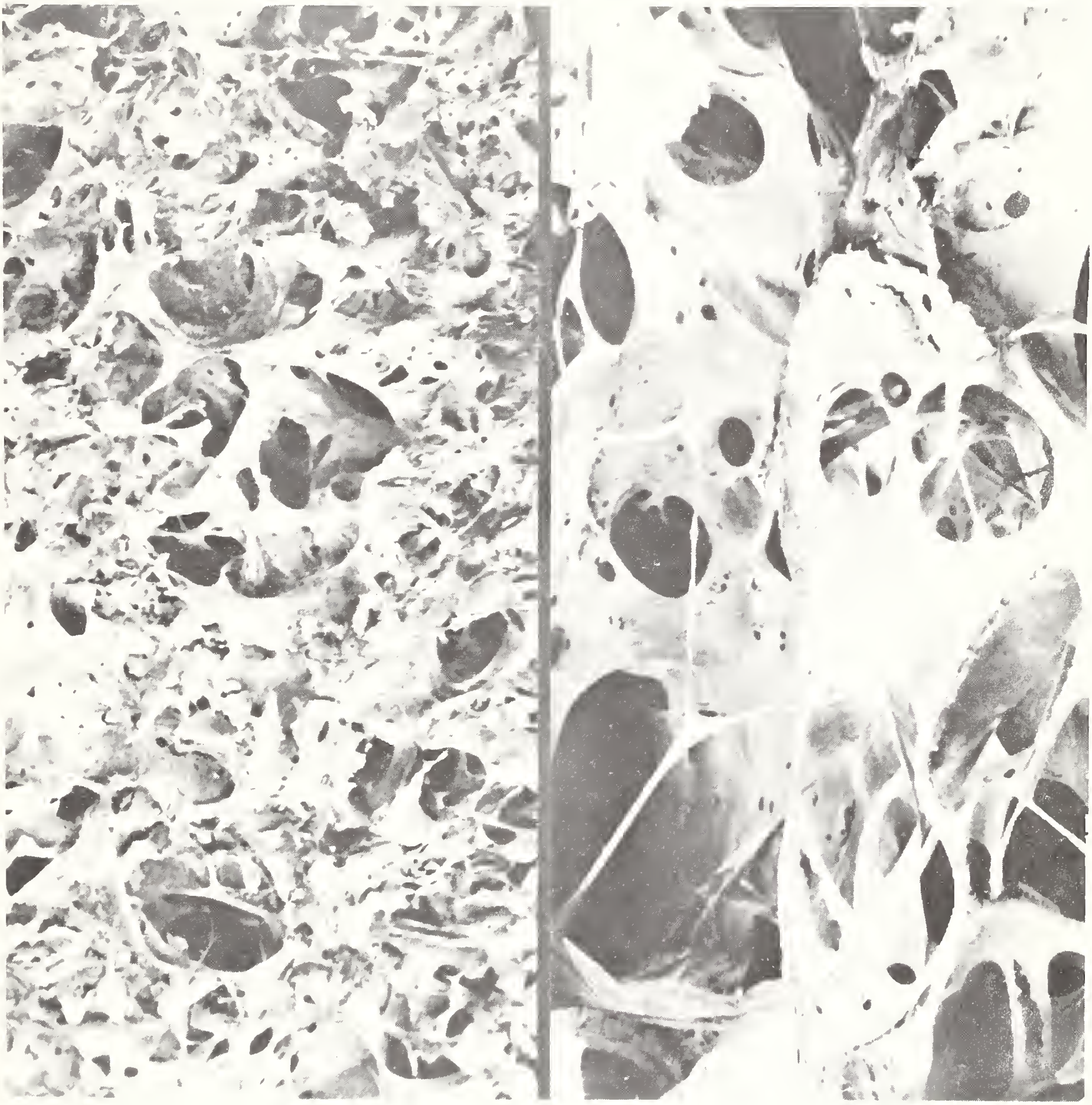

A Medical College of Wisconsin technician, Patricia Delaney, used a scanning electron microscope to show this comparison of a portion of a normal human lung (left) and a human lung with emphysema (right). This photograph and the cover photo were provided by the American Lung Association. (NIH Photo, #1338)

#

News Feature

NEW NCI DIVISION APPLIES PROVED RESEARCH FINDINGS

It is the goal of the recently established Division of Cancer Control and Rehabilitation of the National Cancer Institute to prevent cancer, relieve its effects, and improve the quality of life for its victims through the use of proved research findings that are ready for application in health practice.

Cancer control activities designed to demonstrate the application of specific research advances are implemented through cancer centers, community hospitals, state health departments, voluntary agencies, and other organizations.

The new division is also responsible for research in rehabilitation of cancer patients and the steadily increasing number of long-term cancer survivors.

Several studies on the effect of early detection and treatment of lung cancer are funded by this division. Screening projects at Johns Hopkins University, Baltimore, Maryland, and Memorial Sloan-Kettering Cancer Center, New York City, focus on men 45 to 69 years of age who are regular cigarette smokers, therefore at higher risk of developing lung cancer. Another study at East Texas Chest Hospital, Tyler, Texas, screens almost 900 former asbestos workers who are at excess risk of developing lung cancer and other asbestos-related diseases.

A uterine cervical cancer screening demonstration program aimed primarily at high-risk, low-income women, has been funded with 20 State

(more)

health departments. Pap tests are provided at no charge with follow-up, treatment, continuing care, and rehabilitation when necessary.

The division also funds several breast cancer detection projects designed to demonstrate the life-saving potential of a combination of early detection methods: an annual physical examination; breast X-ray; and thermography, which measures skin temperature patterns. These projects will screen about 270,000 women over 35 years of age.

The most effective treatments for three types of cancer--acute lymphocytic leukemia, Hodgkin's disease, and non-Hodgkin's lymphomas --are being made more widely available through seven cancer control demonstration projects. Recent advances in treatment, particularly with anticancer drugs, have greatly improved survival times for patients with these diseases. These projects demonstrate to physicians and other health workers new methods of determining the nature and extent of each patient's cancer, and in delivering the most effective treatments.

Rehabilitation of cancer patients to restore them to as normal a state of health as possible is a major concern of the Cancer Control Program. The division has awarded contracts to several institutions to develop cancer training programs for physical and/or occupational therapists, as well as development of prosthetic devises.

It is the purpose of the Division of Cancer Control and Rehabilitation to ensure the translation of research findings into practice.

#

News Feature

DRUGS UNDER STUDY FOR TREATING HERPES SIMPLEX KERATITIS

Herpes simplex keratitis, the herpes simplex infection of the cornea, accounts for more sickness and loss of vision than any other corneal infection in the Western countries. It is one of the most difficult corneal diseases to treat because the infection may clear and then recur; therefore, patients afflicted with herpes simplex keratitis fluctuate between periods of pain and relief throughout their lives.

In 1961, Herbert Kaufman, M.D., of the University of Florida, a grantee of the National Eye Institute (NEI), used the antiviral drug idoxuridine (IDU) to cure herpes simplex keratitis. This was the first time a viral infection in the body was cured by medication. However, IDU proved to be ineffective in some therapy, often causing undesirable side effects.

Presently, Dr. Kaufman and other researchers, many working with NEI support, are investigating the use of two new drugs--trifluorothymidine (F_3T) and adenine arabinoside (ara-A)--to treat herpes simplex ulcers of the cornea. Their studies have indicated that both F_3T and ara-A are equal, and in some cases superior, in their therapeutic effects to IDU.

Dr. Kaufman and Barrie Jones, M.D., of the University of London, conducted a study in 1971 comparing the healing ability of IDU with F_3T. At Moorfields Eye Hospital in London and at the University of Florida, patients were treated with one drop of each drug five times daily for two weeks. Results showed that F_3T healed more patients than IDU, and it healed them an average of two days sooner.

(more)

Keratitis (Cont'd)

Researchers studying ara-A indicate also that it is a superior treatment, particularly in dealing with a recurrent disease in patients who are resistant to IDU. The scientists suggest that ara-A is less toxic to the cornea epithelium than IDU and that in many of the patients studied, there was no display of significant toxic reactions.

The investigators appear hopeful that with the use of F_3T, ara-A, and other drugs of therapeutic capability that are currently under investigation, treatment of herpes simplex keratitis will be more successful in the future.

#

HEAD INJURY--The National Institutes of Health is funding several research projects about head injuries, including an investigation of cerebral blood flow during coma and a separate study of recovery after the acute care phase is passed. The knowledge that irreversible brain damage in survivors is usually a result of the aftereffects of the injury rather than the injury itself makes a special effort in this research immensely worthwhile.

Medical News Tip

REMISSION OF JUVENILE DIABETES---A functional recovery of the beta cell and unimpaired insulin sensitivity play a vital role in maintaining the clinical remission of juvenile diabetes. Usually, the onset of the illness is rapid in insulin-dependent, ketosis-prone young diabetics and is accompanied by nearly complete failure of beta-cell function. But in one out of five patients, a temporary remission of diabetes occurs shortly after diabetes begins.

John S. Soeldner, M.D., a grantee of the National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD), investigated why most patients in remission show substantial insulin responses to glucose and to a physiologic meal, and near-normal responses to administration of exogenous insulin.

Dr. Soeldner studied eight nonobese, ketosis-prone juvenile diabetics in remission who could be managed without insulin, and a control group of nonobese healthy volunteers of the same age range. He assessed the secretory capacity with oral glucose, intravenous glucose, and oral mixed meal tests, and insulin sensitivity with a one hour intravenous insulin test.

Results showed that insulin responses in the affected group were variable and relatively subnormal compared to those in healthy control subjects although definite responses to all three stimuli were noted in the majority of patients. The patients also responded to physiologic doses of intravenous insulin with a normal decrease in blood glucose and plasma free fatty acid levels. This suggests maintenance of *in vivo* insulin sensitivity.

For additional information about NIAMDD studies of juvenile diabetes, contact: NIAMDD, Bldg. 31, Room 9A04, Bethesda, MD 20014, phone (301) 496-3583.

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News Releases Issued

EDUCATION PROGRAMS--The National Cancer Institute (NCI) has announced a $4 million Clinical Education Program of grants to stimulate development of more innovative teaching methods in cancer prevention, diagnosis, treatment, and rehabilitation. Eligible institutions include schools of medicine, dentistry, osteopathy, and public health, affiliated teaching hospitals and specialized cancer institutions. The program will improve instruction in cancer-related subjects at both undergraduate and graduate levels. The grants will fund only cancer education activities which are in addition to the existing curriculum. Awards will not include fellowships or other forms of individual stipends. For information, contact: Education Branch, Division of Cancer Research Resources and Centers, NCI, Westwood Building, Room 10A07, Bethesda, Maryland 20014.

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Research Advances

NIH SCIENTISTS DEVELOP TOOL FOR CANCER STUDIES

Using a fast-acting C-type virus called the Abelson leukemia virus, NIH scientists have changed mouse lymphocytes to malignant cells *in vitro*. The malignant cells, when injected into mice of a different genetic strain, then grew into tumors.

Although C-type virus has been associated with lymphomas in several mammalian and avian species, little is known about how it affects lymphoid cells and how it induces tumors. Investigation has been difficult because scientists have been unable to develop an *in vitro* system in which they could be sure that the virus transforms normal cells to malignant ones.

One factor necessary for an *in vitro* system is a fast-acting virus. For most type-C viruses, several months must pass between infection and appearance of a tumor. Another problem has been to find an appropriate cell system that can be kept alive in a culture medium long enough to be infected. And a third problem has been the need to show that a tumor is really from the injected, transformed cells and not a result of viral infection of the recipient's cells or of a graft-versus-host reaction.

The NIH investigators used the Abelson virus, which induces tumors within three to four weeks, to infect spleen cells from mice. The spleen contains lymphocytes that are in different stages of maturation and differentiation, and that can be stimulated to DNA synthesis, necessary for tumor formation. Four to six days later, the infected cultured cells were then transplanted into histocompatible mice with a karyotype different from that of the donor so that the origin of the tumor cells could be determined.

(more)

Cancer Studies (Cont'd)

Since malignant tumors developed that contained donor cells, the scientists conclude that transformation had taken place *in vitro*.

This *in vitro* system provides a new tool that can be used to study how the type-C virus affects particular cell components and functions, and other aspects of viral transformation that are impossible to study *in vivo*.

Marshall D. Sklar, M.D., of Stanford University Medical School, Beverly J. White, M.D., of the National Institute of Arthritis, Metabolism, and Digestive Diseases, and Wallace P. Rowe, M.D., of the National Institute of Allergy and Infectious Diseases (NIAID) reported their findings in the October issue of the *Proceedings of the National Academy of Sciences*. Dr. Sklar was formerly with NIAID.

#

PAIN RELIEF--Electroanesthesia is a promising method of easing pain which will require much more research before it can be recommended, according to the National Institutes of Health. Some European dentists find that when they pass a small current from a battery through an insulated dental drill into a tooth and return the current to its source via a wire attached to a metal clip on the patient's ear, the sensation of drilling is blocked.

#

Research Advances

WEIGHT FLUCTUATION ENHANCES GALLSTONE RISK IN OBESITY

Obese individuals who are subject to gallstones are even more susceptible during a period of weight reduction and should, therefore, avoid alternately losing and regaining weight, according to scientists whose work was funded by the National Institute of Arthritis, Metabolism, and Digestive Diseases.

It is well-known that the obese tend to have gallstones more frequently than lean persons and that weight reduction and maintenance of normal weight diminishes the risk of developing such accretions. Recent research has linked cholesterol gallstone formation to hepatic secretion of bile supersaturated with cholesterol (lithogenic bile). The specific relationship, however, between obesity and bile lithogenicity has not been fully explored.

Studies of gallbladder bile from the obese now have revealed that bile lithogenicity is consistently increased in the obese state, and increased even further during weight loss. Once weight is stabilized at a lower level, however, bile is consistently less lithogenic. Thus, the obese person who alternately loses and regains weight and does so frequently and repeatedly throughout life may intensify the risk of developing gallstones.

Analysis of gallbladder bile from 17 obese and 17 lean subjects showed that bile from obese subjects is significantly more saturated with cholesterol. Before weight reduction, such bile had a mean molar percent cholesterol of 12.4; after an average weight loss of 24 kg, the average molar percent cholesterol dropped markedly, to 7.2.

Further analysis of secretion rates of cholesterol, bile acid, and lecithin (phospholipid) before and after weight reduction revealed that only

(more)

cholesterol secretion changed significantly with weight loss, decreasing by 24 percent. A novel finding was that bile lithogenicity increased in five of 10 obese patients while they were losing weight.

Lynn J. Bennion, M.D., and Scott M. Grundy, M.D., reported their findings to the annual meeting of the American Federation for Clinical Research and the American Society for Clinical Investigation. In a complementary study reported by Paul H. Schreibmann, M.D., of Rockefeller University, bile lithogenicity rose markedly in four of five hospitalized obese patients during a period of weight reduction.

#

FLUORIDE VALUE--Many things contribute to tooth decay including heredity, foods, frequency of eating, bacteria in the mouth, saliva, and access to certain trace minerals. Nevertheless, drinking properly fluoridated water consistently and safely reduces decay by about 60 percent, according to the National Institutes of Health.

CATARACT SURGERY--It is no longer considered necessary to wait until a cataract is ripe to perform surgery. This was common practice at one time, but cataract operations can now be performed successfully even when the patient still maintains a fair amount of vision, according to the National Institutes of Health.

#

Research Advances

NEW PROCEDURE MAY "CLEAN" BLOOD OF SPECIFIC ANTIBODY

Circulating antigens and antibodies, which seem to play a role in cancer and autoimmune diseases, might be removed from a patient's blood through use of a mechanical method recently developed by grantees of the National Institute of Allergy and Infectious Diseases. The new procedure--carried out to date only in dogs--involves: (1) chemical binding of specific antigen to nylon tubing; and (2) inserting the treated tubing in a major vein channel. Using this procedure, the scientists have been able to remove significant amounts of specific antibody from an animal's circulating blood.

Circulating antigens, antibodies, or both, are believed to interfere with the immune defenses of a cancer patient and thus make it difficult for the body to destroy malignant cells. Complexes of antigen and antibody may also deposit in clusters of kidney blood vessels resulting in kidney failure in some patients with the autoimmune disease, systemic lupus erythematosus (SLE). Safe removal of these immune complexes of SLE or the blocking factors in cancer could be an important addition to other means of immunotherapy.

The scientists, Leon R. Lyle, M.D., Brent M. Parker, M.D., and Charles W. Parker, M.D., at the Washington University School of Medicine, St. Louis, were able to chemically bind two common proteins--human serum albumin and chicken egg albumin--to separate samples of nylon tubing. A mixture of antisera to the two proteins (each of which had been labelled with different radioactive isotopes) was injected into the dogs, and, after 10 minutes, the tubing was inserted for various lengths of time into the inferior vena cava

(more)

Antibody (Cont'd)

of the anesthetized dogs. Measurements of the amount of radioactivity bound by each tubing showed that even more antibody was specifically removed from the dogs' blood in this *in vivo* test than when the tubing had been tested *in vitro* (outside the body).

Based on their findings, the researchers estimate that 500 micrograms of antibody could be removed in 24 hours of exposure to the tubing. Since less than 500 micrograms of tumor-associated antigen is estimated to be present in blood of patients with certain forms of cancer, semi-continuous use of tubing to which specific antibody had been bound should remove such antigen.

The Washington University group did not detect any leakage of the bound antigen from the tubing in their experiments. If bound protein (antigen or antibody) did leak into the body tissue, serious immune reactions could occur with the possible production of tissue damage or shock. Careful evaluation of the stability of the chemical bond is strongly advised before this or any other new binding procedure is applied clinically.

The scientists reported their new method in the August 1974 issue of *The Journal of Immunology*.

#

Research Advances

"Pharmacologic" Doses...

VITAMIN C CAN DESTROY VITAMIN B_{12} IN FOOD

A grantee of the National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD) has shown that "pharmacologic" doses of vitamin C destroy substantial amounts of vitamin B_{12} contained in food. This effect is unequivocal, while the value of such doses of vitamin C in preventing the common cold is highly uncertain.

High doses of vitamin C, in the gram range, are popular as a home remedy against the common cold. The investigators recently observed that four of nine paraplegic patients taking 1 gm vitamin C daily had low serum vitamin B_{12} levels. Additionally, other scientists reported in 1956 that vitamin C exerts a destructive effect on crystalline vitamin B_{12}, which is more stable than the forms naturally present in food.

It is now reported that high doses of vitamin C destroy substantial amounts of vitamin B_{12} when ingested with food. The findings enlarge the list of possible and probable adverse effects of large doses of vitamin C, and suggest that daily ingestion of 0.5 gm or more without regular evaluation of vitamin B_{12} status is probably unwise and might result in anemia.

To mimic meal ingestion *in vitro*, meals with a modest and a high vitamin B_{12} content were homogenized in a food blender, incubated for 30 minutes at 37°C after addition of varying amounts of vitamin C, and then assayed for vitamin B_{12} content. Cottage cheese was the principal source of B_{12} in the "modest B_{12} meal," while beef liver was the principal source in the "high B_{12} meal."

(more)

Vitamins (Cont'd)

The vitamin B_{12} content of the "modest B_{12} meal" was decreased 43 percent by 0.1 gm, 81 percent by 0.25 gm, and 95 percent by 0.5 gm vitamin C. By contrast, 0.1 gm vitamin C had a minimal effect on the B_{12} content of the "high B_{12} meal," while 0.25 gm vitamin C destroyed 25 percent of the B_{12} and 0.5 gm destroyed less than 50 percent. Preliminary investigations suggest that the Recommended Daily Allowance of 45 mg vitamin C does not destroy vitamin B_{12} in food.

It has been reported that iron stabilizes vitamin B_{12} activity in liver extracts, thus the iron content of a meal may influence the destruction of vitamin B_{12} by vitamin C. In the present study, beef liver iron apparently reduced the damaging effect of vitamin C on vitamin B_{12}. NIAMDD grantee Victor Herbert, M.D., of Columbia University and his associate Elizabeth Jacob, M.D., reported their study in the *Journal of the American Medical Association*, Vol. 230, No. 2, pp. 241-242.

#

TOOTH DECAY--Grinding surfaces of teeth are especially susceptible to decay because many have small irregularities. These pits and fissures make thin spots in the tooth enamel that trap food, bacteria, and enamel-dissolving acids derived from bacterial fermentation. Many of these crevices are too small for toothbrush bristles to scour, according to the National Institutes of Health.

#

Photo Feature

WATER POLLUTION PRESENT IN ROCKY MOUNTAIN WATERWAYS

Researchers indicate that automobile exhaust is the cause of lead contamination in the Rocky Mountain lakes and streams of northeastern New Mexico. In the Pecos Wilderness, a desolate area at the foot of the Sangre de Cristo mountain range, members of a scientific task force found minute particles of lead in water samples taken from this region during the past three years. Their studies show the primary source of lead impurities in the waters is airborne particles resulting from car exhaust emission which is subsequently deposited by precipitation.

Even though the Pecos Wilderness is removed from metropolitan areas, contamination apparently drifts in from high pollution areas.

Chemical analyst Sigfredo Maestas, Ph.D., director of the study project, cautions, however, that the finding does not place New Mexico in a critical public health situation. The lead levels examined are 100 to 1,000 times less than the allowable level in drinking water--50 parts per billion.

The research staff are participants in the NIH Minority Biomedical Support Program at the New Mexico Highlands University of Las Vegas, New Mexico. The purpose of the study is to determine the content, distribution, and origin of the lead present in surface and ground water of northeastern New Mexico. The undergraduate scientists are also developing suitable sampling techniques, and designing statistical means of determining the origin by which lead occurs in the samples.

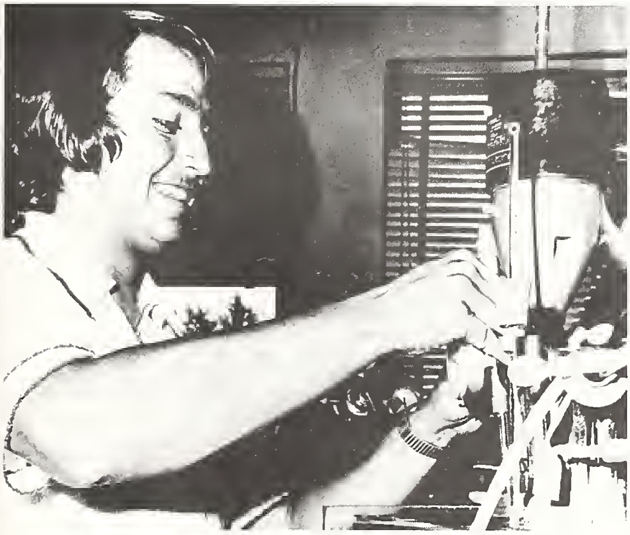
Situated at altitudes of from 6,500 to 13,000 feet, the Pecos Wilderness is considered one of the cleanest in the country from an ecology standpoint.

(more)

Pollution (Cont'd)

Lead contamination statistics from these studies have been filed with the New Mexico Water Resources Research Institute for comparison with findings in waters adjacent to metropolitan areas. These statistics are also intended to serve as a base for future monitoring of lead contamination in this area. The researchers feel that the Pecos Wilderness lead levels in water may possibly serve as a barometer for the rest of the nation.

The study is supported by the Division of Research Resources and the New Mexico Water Resources Research Institute.



Chemical analysts use an electrochemical technique to determine the level of lead contamination in the waters of the Sangre de Cristo mountain range. Researcher Donald H. Virgil uses an anodic stripping voltanimetry process to analyze for metals in electrolytic solutions. (NIH Photo #1339)

Undergraduate investigators participating in the Minority Biomedical Support Program backpack 10 to 15 miles into the Pecos Wilderness to gather the samples. Kenneth Padilla holds plastic jars containing the water collected from the mountain lakes and streams. (NIH Photo #1340)

#

News Feature

NINDS STUDIES LEAD TO SOME "NEW" DISORDERS

The more we learn, the more we need to learn.

Scientists working for the National Institute of Neurological Diseases and Stroke (NINDS) recently have discovered some previously-unreported disorders that will require further study.

One of two disorders found in 1972 is named benign congenital hypotonia, a non-progressive muscle disorder with Type II fiber predominance. The other is a syndrome characterized by abnormalities in the muscle fibers in conjunction with paralysis of the eye muscles. The scientists call this disorder oculocraniosomatic neuromuscular disease with ragged red fibers.

Then in 1973 scientists reported observing similar abnormal muscle fibers in a new hereditary syndrome consisting of limb-girdle dystrophy, myocolous epilepsy, and elevated lactates and pyruvates that can be fatal in childhood.

Also in 1973, a rare myopathy carnitine deficiency, was described by NINDS grantee investigators in Minnesota. Carnitine, a component of muscle tissue, seemed to be absent in the skeletal muscle of a patient with progressive muscle weakness. Prednisone therapy improved the patient's weakness. Scientists hope to find the cause of carnitine deficiency.

In still other NINDS research in 1973, scientists were surprised by a finding from their investigation of myophosphorylase deficiency. They were able to provoke production of the enzyme myophosphorylase in the muscle fibers of patients suffering from this deficiency. The "revival" of this enzyme, which is essential in sugar metabolism, occurred when the muscle cells were regenerating after injury. Previous thinking held that the enzyme was

(more)

genetically absent.

It is now hoped that therapeutic efforts can be directed toward promoting production and retention of myophosphorylase in mature fibers. It is possible that this approach could also apply to other genetic enzyme deficiencies.

#

TWO "PLAQUES"--Dental plaque is an "invisible" sticky bacterial film that forms on teeth. It is composed of material from saliva and bacteria and their products. Failure to remove plaque may lead to tooth decay. Also, plaque may gradually mineralize into calculus, or tartar, the hard deposit that forms on the crown surfaces of the teeth or the root surfaces beneath the gum margins. Removal of calculus is important because it may be a forerunner of gum trouble, according to the National Institutes of Health. In hardening of the arteries, plaque is the buildup of fatlike substances on the inside walls of the arteries. This accumulation forms thick deposits, making it more difficult for enough blood to get through the artery. Every artery throughout the body is subject to hardening, but the most often and most seriously affected vessels are the largest arteries, such as the aorta, the coronary arteries, and the arteries that feed the brain and kidneys.

#

Photo Feature

SCIENTISTS COMMUNICATE BY NASA SATELLITE

Via a NASA satellite, scientists at the National Institute of Allergy and Infectious Diseases (NIAID) maintain contact with their research teams in the Pacific area. The isolated-site scientists can also talk to any other scientists in the continental U.S.A. via telephone connections through the NIAID office. The system allows conversation three times a week by direct radio-telephone hook-up to the ATS-1 satellite communication system.

The network also enables the parties to hold conferences as well as provides swift communication in an emergency.

Dr. Earl C. Chamberlayne is project officer for the satellite telecommunication feasibility study which was initiated by NIAID in July 1973 and is designed to determine the benefit of satellite communication for biomedical research. A control panel located in Dr. Chamberlayne's office includes a remote operating console, speaker, and monitor that ensures the sender his message is being transmitted.

Dr. Chamberlayne hopes the satellite communication will facilitate discussions and provide immediate feedback for an increasing number of scientists who are separated from each other by many miles. Dr. Chamberlayne talks from his office on the NIH campus with Rarotonga, Cook Islands, in the South Pacific where some NIAID investigators are conducting studies on filariasis. (NIH Photo #1341)

Investigators in the field sites use simple, portable sets which are transistorized FM radios carrying crystals for appropriate frequencies for satellite use.

(more)

Satellite (Cont'd)

The ATS-1 satellite, in stationary orbit, can transmit voice, facsimile images, and digital data such as those sent across telephone lines from one computer to another. ATS-1 uses energy provided by solar cells on board.

The project is under the supervision of the Lister Hill National Center for Biomedical Communications, National Library of Medicine (NLM). The base station equipment for the Bethesda site is also located at NLM.

#

WASTING DISEASE--Muscular dystrophy (MD) usually begins in childhood but it can attack persons of all ages. It affects over 200,000 people in the United States, according to the National Institutes of Health. MD is a progressive, wasting disease that weakens the "voluntary" or skeletal muscles--those on the "outside" of the body--such as the biceps that youngsters show by flexing their arms.

MUSCULAR DYSTROPHY--The most prevalent form of muscular dystrophy (Duchenne) is a sex-linked, genetic trait carried by women who show no symptoms themselves. There is, however, a 50 percent chance that male offspring will be afflicted, and a 50 percent chance that female offspring will be carriers, according to the National Institutes of Health.

#

News Feature

MIAMI SERVES AS SITE FOR PRIMATE COLONY

The NIH Perrine Primate Center is a breeding colony for rhesus and squirrel monkeys located on a 60-acre preserve near Miami, Florida. Under the direction of the Veterinary Resources Branch of the Division of Research Services (DRS), an NIH staff of four individuals routinely check the primates to insure healthy breeding stock.

NIH scientists require approximately 3,000 monkeys annually. Previously, the chief source of primates was India, but the country has placed an embargo on rhesus in an attempt to conserve the natural resources. Export has been cut approximately in half. Squirrel monkeys from South America are also hard to get. It was of necessity, therefore, that domestic breeding colonies be established.

Rhesus are shipped from India to the NIH Animal Center in Poolesville, Maryland,where they are quarantined for 120 days. Those selected for Perrine are flown to Miami and transported to the Primate Center in air-conditioned trucks.

The issuing of timed pregnant rhesus monkeys to NIH scientists is also a part of the Veterinary Resources Branch breeding program. After conception, which is known within 72 hours, the animals are used for studies that require an unborn or newborn rhesus. These involve such areas of research as fetal development and early pregnancy diagnosis. The scientists of DRS and the animal technicians at Perrine see the Primate Center as an important laboratory for breeding the monkeys which are so essential for NIH intramural research, while conserving the wild primate populations.

#

News Releases Issued

MINORITY SUPPORT--Two-year colleges, native American Indian Tribal Councils, and institutions with significant enrollment from ethnic minority groups will be eligible for research support from NIH, according to proposed regulations published on December 30, 1974, in the *Federal Register*. The regulations would broaden the Division of Research Resources' Minority Biomedical Support Program, which is designed to encourage greater participation by minority group members in biomedical research. Under the Program, grants are awarded for this purpose to predominantly minority colleges.

DIABETES RESEARCH--The National Institute of Arthritis, Metabolism, and Digestive Diseases has awarded $4 million in grants to establish four Diabetes-Endocrinology Centers to expedite the flow of new scientific information from the laboratory to patient care. The Centers, whose grants vary from three to five years, are at the University of Virginia, Charlottesville; Vanderbilt University, Nashville; the University of Chicago; and the University of Washington, Seattle.

#

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Research Advances

NEW PAPOVAVIRUS FOUND ASSOCIATED WITH WISKOTT-ALDRICH SYNDROME

NIH scientists have reported the isolation of a new papovavirus from the urine of three out of three Wiskott-Aldrich patients studied at the NIH Clinical Center. In one of these patients, the virus was also found in cultures of the brain tumor which contributed to his death.

A direct relationship of the virus to the tumor has not been established. This work, however, has excited scientists engaged in virus-cancer research since several members of the papovavirus family are known to cause tumors in laboratory animals.

The Wiskott-Aldrich syndrome is a sex-linked recessive disorder in which patients with the disease have immunologic defects and a high cancer rate. For example, malignancies of the reticuloendothelial (blood-forming) system occurred in six of 13 boys with the Wiskott-Aldrich syndrome studied at NIH since 1966.

When one of these children developed a brain tumor, virologic and tissue culture studies of the excised tumor were undertaken by National Institute of Allergy and Infectious Diseases (NIAID) and National Cancer Institute (NCI) scientists. After six weeks, cultures containing tumor fragments underwent changes reminiscent of those seen in cultures infected with the papovavirus known as BKV. This virus, found frequently in the urine of immunosuppressed kidney transplant patients, cross-reacts with SV40, the well-studied monkey papovavirus which causes tumors in newborn hamsters.

Further laboratory tests strengthened the NIH investigators' suspicion that they had isolated, in the tumor fragment culture, an agent similar to

(more)

BKV, although electron microscopic examination of the tumor tissue itself did not reveal viral particles. Subsequent serologic tests proved that the new isolate was closely related to BKV and not SV40.

When the scientists purified the new virus found in the cultured tissue and examined it by electron microscopy, a typical papovavirus structure was seen.

Serum samples collected over a three-year period from the brain tumor patient were next tested for antibody to the new agent (known as MAM) and to BKV. A dramatic rise in antibody titer to both viruses was found to have occurred in the patient's serum as long as a year before clinical signs of the brain tumor were noted. Five serum samples taken after discovery of the brain tumor showed a decrease in titer but the antibody level remained high.

The continued high antibody levels suggested a persistent infection and led the scientists to search for virus in the urine of the patient. Samples of urine were collected, spun into pellets, and examined by electron microscopy. Large numbers of virus particles typical of the papovaviruses were found.

During the course of these studies, the NIH scientists detected papovaviruses in the urine of two other Clinical Center patients with the Wiskott-Aldrich syndrome. Like the first case, these patients also developed rises in serum antibody titer to BKV and MAM. One of the patients has now developed cancer and is being carefully studied.

This work was reported in the November issue of the *Journal of the National Cancer Institute* by Kenneth K. Takemoto, Ph.D., Michael F. Mullarkey, M.D., and Claude F. Garon, Ph.D., of NIAID, and by Alan S. Rabson, M.D., and R. Michael Blaese, M.D., of NCI.

#

Research Advances

SCIENTISTS INVESTIGATE MUCUS TRANSPORT IN CYSTIC FIBROSIS

Scientists of the National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD) have demonstrated decreased mucociliary transport in cystic fibrosis. The investigators also found that its stimulation by a pharmacologic agent, terbutaline, may have therapeutic significance.

Much of the therapeutic effort in the inherited metabolic disease cystic fibrosis (CF) is directed toward chronic lung disease, the severity of which usually determines the CF patient's fate. Although aerosols, mist tents, mucolytic agents, and postural drainage are used with some success in removing mucus from the lungs, an effective means of increasing airway clearance pharmacologically would be an advance in the treatment of CF.

The present research has demonstrated that tracheal mucus velocity, as a measurement of mucociliary airway clearance, is markedly decreased in CF patients. Administration of a new beta-adrenergic agent, terbutaline, significantly increases tracheal mucus velocity and, so this pharmacologic agent may be of therapeutic importance in CF.

Tracheal mucus velocity was measured by observing the motion of Teflon discs across the tracheal mucosa through a transnasally-introduced fiber-optic bronchoscope. Such measurements were obtained in 14 adult CF patients and in 20 normal volunteers of the same age. The studies then were repeated in the 14 patients and in 10 control subjects after subcutaneous injection of 0.25 mg terbutaline.

The average mucus velocity in 14 CF patients was less than 15 percent of that in the 20 control subjects. Following terbutaline administration, average

(more)

mucus velocity more than doubled in the CF patients, but was relatively unaffected in the control subjects. Side effects of terbutaline were minimal and transitory, and several patients reported a marked increase in sputum production for several hours after the study.

These findings suggest that severe impairment of mucociliary transport may play a role in the pathogenesis and chronicity of pulmonary disease in CF. Although the mechanism by which terbutaline acts to increase such transport is unknown, this marks the first quantitative demonstration of pharmacologic improvement in mucociliary transport in CF.

Robert E. Wood, M.D., Ph.D., and Philip M. Farrell, M.D., Ph.D., of the NIAMDD's Pediatric Metabolism Branch, and associates at the National Heart and Lung Institute and Mount Sinai Medical Center, Miami, reported their findings before the recent annual meeting of the Society for Pediatric Research in Washington, D.C., and an abstract of their paper appears in *Pediatric Research*, Vol. 8, pg. 471 (1974).

#

AGING RESEARCH--The search for more knowledge about aging has intensified in recent years. This quest is important because 21 million people, about 10 percent of the American population, is now 65 years of age or older and the number is steadily increasing, according to the National Institutes of Health.

#

Research Advances

IMPROPER CATHETER MAINTENANCE MAY CAUSE URINARY TRACT INFECTIONS

Failure of hospital staff to adhere strictly to sterile techniques in the care of catheterized patients may be responsible for the continued high incidence of urinary tract infection in these patients, according to a study funded by the National Institute of Allergy and Infectious Diseases. Results of their study also confirmed previous findings that women and elderly, or critically-ill patients have a high risk of acquiring bacterial urinary tract infections.

Catheter-associated urinary tract infections are the most common type of hospital-acquired infections, resulting in morbidity, prolonged hospitalization, and death. Ten years ago, it was found that use of a urethral catheter connected to a closed sterile drainage bag could reduce such infection rates from 80 percent to less than 10 percent. Today, however, more than 20 percent of hospital patients receiving this type of catheterization continue to develop bacterial infections.

To determine the reason for this continuing problem, researchers at the University of Utah and Salt Lake City Latter-Day Saints Hospital followed 405 carefully screened patients, whose median duration of catheterization was two days. More than 23 percent of the patients developed urinary tract infections with *E. coli*, enterococci, pseudomonas, klebsiella, enterabacter, and proteus organisms. The daily rate of infection with these organisms increased as the length of catheterization increased, reaching 50 percent in those catheterized for 10 days or more.

(more)

Catheters (Cont'd)

There was a lower incidence of bacteria in the urine if a doctor or registered nurse, rather than a practical nurse, inserted the catheter. Technical errors, such as improper positioning of the drainage bag, and frequent breaks of the catheter-tubing junctions, played a major role in allowing bacteria to enter the drainage system and colonize the bladder urine.

Because of their findings, the Salt Lake City group recommends careful weighing of the risks and benefits of catheterization in a high-risk patient and removal of indwelling catheters as early as possible. The researchers also verified other reports that antibiotics lower infection rates only during the first four days following catheterization. After this time, the drugs may contribute to further development of resistant hospital bacteria.

The researchers Richard A. Garibaldi, M.D., John P. Burke, M.D., Marion L. Dickman, M.D., and Charles B. Smith, M.D., reported their study in the August 1, 1974 issue of *The New England Journal of Medicine*.

#

SALIVA SERVICES--Although taken for granted or ignored by most people, saliva gives us valuable silent services. Perhaps its most vital role is to moisten foods for swallowing. Another function is to begin the digestion of starch. Saliva also helps protect teeth from decay-causing bacterial acids, and washes away unattached bacteria that can cause disease, according to the National Institutes of Health.

#

Research Advances

SCIENTISTS ISOLATE TWO PROTEINS RESPONSIBLE FOR FEVER IN HUMANS

Significant progress in understanding the production of fever in humans has been achieved by the first isolation of two chemically and biologically distinct fever-causing substances released by two different cell types. According to National Institute of Allergy and Infectious Diseases (NIAID) scientists, one of these substances is produced in greater quantities by fewer cells than the other and induces a fever which peaks later but lasts longer.

Fever is thought to be caused by a protein, leukocytic pyrogen, released by white cells when they ingest bacteria, bacterial products, or other foreign particles. In the laboratory, neutrophils, the most abundant human white cells, have been shown to release this protein upon exposure to bacteria, as have monocytes, white cells which also destroy bacteria.

The NIAID researchers, Charles A. Dinarello, M.D., Nathan P. Goldin, and Sheldon M. Wolff, M.D., of the Laboratory of Clinical Investigation, refined crude separations of neutrophils and monocytes from samples of human blood and incubated each cell type with killed staphylococci. The monocytes released 20 times as much pyrogen as did the neutrophils.

Each of the proteins was then injected into rabbits and produced fevers in the same amount of time. However, the neutrophil protein produced a fever which peaked at 40 minutes. The fever caused by the monocyte protein did not peak until 60 minutes but remained elevated for a longer time than did the fever produced by the neutrophil pyrogen. There are also striking chemical differences between the two molecular forms of pyrogen.

(more)

The scientists feel that the difference in fever peaks could indicate that the proteins act on separate sites of the hypothalamus, that part of the brain which controls the body's temperature. In addition, the larger molecule released by the monocytes could exert its effect by remaining in the circulation for a longer time.

The finding that two cell types are producing chemically and biologically distinctive pyrogens may help explain some of the different patterns of fever seen from a wide variety of causes in human beings.

This work was presented at the annual meeting of the American Society for Clinical Investigation in Atlantic City, N.J. in May 1974, and published in the June 1974 issue of *The Journal of Experimental Medicine.*

#

ALLERGY PROBLEM--The symptoms of all allergies are caused by the body's abnormal response to foreign substances called allergens. Each time a person is exposed to the allergen, the irritating allergy symptoms appear, according to the National Institutes of Health. If a person is troubled by bothersome symptoms and suspects he may have developed an allergy, he should consult his family doctor or an allergist, a physician specializing in allergies.

#

Photo Feature

BIOMEDICAL RESEARCH RELIES ON UCLA COMPUTER FACILITY

Today's scientists are finding that one of their greatest needs is for an integrated and automated approach to analysis of medical research data. The University of California at Los Angeles Health Sciences Computing Facility recognizes this and is developing new statistical and mathematical approaches that allow the biomedical scientist to work with the human body's infinite number of variables. The Facility, supported by the NIH Division of Research Resources, is dedicated to bringing the biomedical research worker as close as possible to mathematics, statistics, and computers.

The Facility's IBM 360/91 computer enables the investigator to create, maintain, and use large file systems. In addition, the center's computer programs are designed for the non-computer-system-trained scientist.

A terminal support system (TORTOS) also permits the researcher to converse with the computer from a terminal located in his office and laboratory while the machine is serving 40 or more other terminals.

Many users receive advice on experimental design, data management, submission of programs, and interpretation of output. Staff collaboration with scientists also takes place on new statistical or mathematical research important to the life sciences.

Carol Newton, Ph.D., uses the computer to support radiation treatment planning and to aid in understanding the mechanisms of the body's cellular system. Dr. Newton devised a mathematical model with graphic display output that allows the therapist to visually observe simulated life cycles of both the normal and malignant cellular population as the treatment progresses. (NIH Photo #1342)

(more)

Anne Spence, Ph.D., works with an autistic child while looking for new genetic factors of the disease. Among those being investigated are the ridge systems at the base of each finger and the dermal ridges of the fingertips. Dr. Spence uses the Health Sciences Computing Facility to help her with the vast amount of multifactorial data she collects on the generations of families she studies. In the above right picture, she uses a remote terminal in her office that aids her in developing models of genetic patterns. (NIH Photos #1343, 1344)

#

TRAINING PROGRAMS--The National Cancer Institute (NCI) is stimulating the widespread application in medical practice of knowledge about cancer prevention and management. Part of the NCI Cancer Control Program involves establishing training programs for nurses and technicians so that these medical personnel will be better able to handle cancer screening, treatment, and rehabilitation services.

#

News Feature

DENTISTS CREDIT FLUORIDE FOR TOOTH DECAY REDUCTION

America's dentists give greater support to water fluoridation than to any other measure for having significant value as a tooth decay preventive, according to a survey by the American Dental Association Research Institute.

About 63 percent of the dentists surveyed believe there has been an overall reduction in the incidence of tooth decay among children in their communities in the past five years.

Community water fluoridation was the chief reason for this reduction, according to half the dentists who participated. About 16 percent of the dentists accorded the reduction to better patient education. Topical fluoride applications were given as the reason by nine percent of the dentists. Three percent of the dentists surveyed credited the use of fluoride dentifrices.

Despite the low number of dentists who rated fluoride toothpastes as having a major impact on the overall reduction of tooth decay, 53 percent of the dentists said fluoride toothpastes are of "moderate value" and approximately 65 percent said they do advise all of their patients under 18 years to use a fluoride dentifrice.

When asked their opinions on specific procedures, 85 percent of the dentists described water fluoridation as having "great value." Other measures described as being valuable were: the restoration of carious lesions, 79 percent; oral hygiene education, 71 percent; formal recall of patients for regular care, 58 percent; nutritional counseling, 56 percent; and prophylaxis, 38 percent.

The study was supported by the National Institute of Dental Research.

#

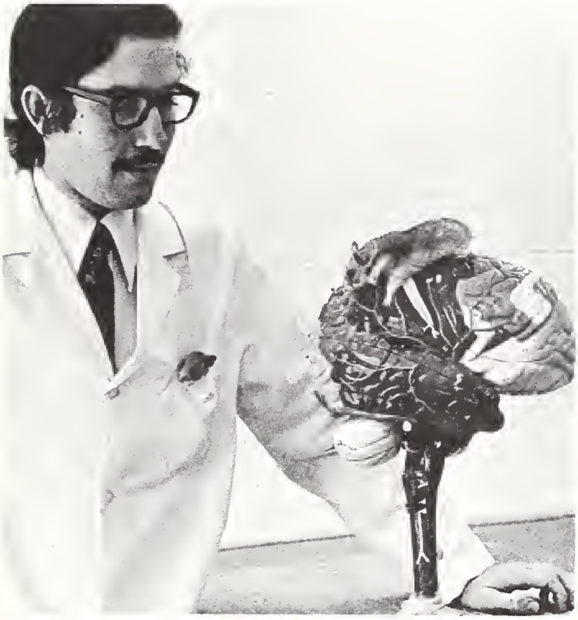
Photo Feature

NEW SYRIAN HAMSTERS AVAILABLE FOR STUDY

Three recently domesticated species of hamsters, captured in their native habitats in Syria, Rumania, and Turkey, have a new home at the National Institute of Mental Health (NIMH) Laboratory of Brain Evolution and Behavior at the NIH Animal Center, Poolesville, Maryland.

Scientists are studying the neuromechanisms of social behavior in these animals. Hamster social behavior is particularly dependent on the sense of smell which is anatomically and physiologically linked to the brain areas known to be important to social behavior. Because of this feature, the hamster provides the investigator with an excellent subject for his research.

These three species of hamsters, which scientists hope will serve as new animal models, were brought to Poolesville by Michael R. Murphy, Ph.D., an NIMH Staff Fellow.



A Turkish hamster investigates a model of the human brain while a Syrian hamster comfortably watches from Dr. Murphy's pocket. Golden hamsters (Mesocricetus auratus) *first came to the attention of scientists in 1839 when G.R. Waterhouse, M.D., of the London Zoological Society, wrote about catching one in Syria. Interest in the animals subsided until 1930 when Israel Aharoni, Ph.D., traveled to Syria and succeeded in capturing a litter. In 1971, Dr. Murphy made the third successful capture of the wild Syrian hamsters, the descendants of which comprise part of his current colony. (NIH Photo # 1345)*

#

Photo Feature

NLM EXHIBIT ILLUSTRATES CAREERS OF "HOPKINS FOUR"

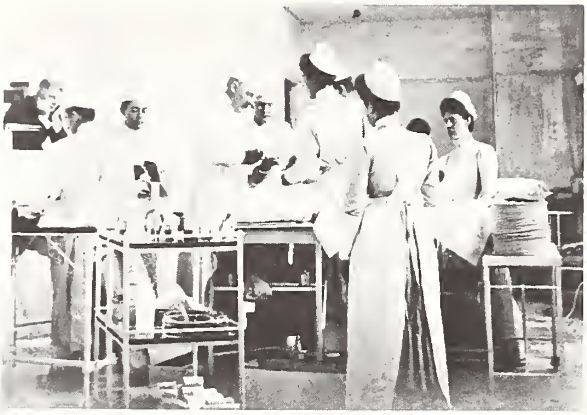
The current exhibit at the National Library of Medicine (NLM) examines the careers and major contributions of four of America's most revered physicians by viewing them through the eyes of their contemporaries. In the process, some little known facts and personal idiosyncrasies come to light. The exhibit portrays their foibles, not to ridicule them, but to demonstrate their very human qualities.

The physicians, William Osler, William S. Halsted, William H. Welch, and Howard A. Kelly, were known as the "Hopkins Four." As the first professors of medicine, surgery, pathology, and gynecology at Johns Hopkins, their combined talents were responsible in great part for the excellent reputation gained by the Johns Hopkins Hospital (opened in 1889) and the Johns Hopkins School of Medicine (opened in 1893).

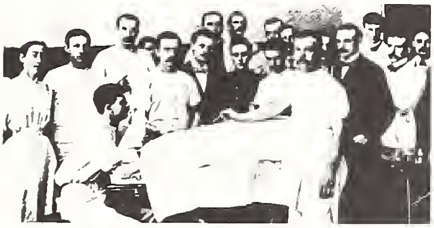
"The Four Physicians," a portrait of Welch, Halsted, Osler, and Kelly (left to right), was painted by John Singer Sargent in 1905. (NIH Photo #1346)

"Hopkins Four" (Cont'd)

"Some Welch Rabbits," by Max Broedel in 1910, depicts William H. Welch, first Professor of Pathology at the Johns Hopkins with many of the outstanding men who trained with him. (NIH Photo #1348)



William S. Halsted (1852-1922), first Professor of Surgery at the Johns Hopkins, prepares for surgery in 1904. Notice caps, gowns, and rubber gloves were routinely worn, but not surgical masks. (NIH Photo #1347)



Howard A. Kelly (left photo) (1858-1943), first Professor of Gynecology at the Johns Hopkins, prepares to operate in the early 1890's. (NIH Photo #1349)

William Osler (1849-1919), first Professor of Medicine at the Johns Hopkins, originated the residency system as we know it today. (NIH Photo #1350)

"The Saint-Johns Hopkins Hospital," a cartoon drawn by Max Broedel in 1896, depicts a cherubic William Osler riding a cyclone above the Johns Hopkins Hospital. Numerous bacteria are retreating. (NIH Photo #1351)

#

New Publication:
Torsion Dystonia

Torsion dystonia is a prolonged and often incapacitating neurologic disorder causing bizarre involuntary movements in its victim's arms, legs, head, and torso. If these movements are maintained for a prolonged period of time, they can result in deformities by causing tendons to shorten and connective tissue to build up in the muscle.

Dystonia has been classified into three types. The recessively inherited form results when both parents, who appear normal, carry a defective gene and pass it on to their child. This form was recently confirmed by scientists who are studying dystonia at the National Institute of Neurological Diseases and Stroke (NINDS). It is found most often in persons of Ashkenazic Jewish (eastern European) ancestry. Persons with this type of dystonia may have higher than normal intelligence, suggesting that the gene for recessive torsion dystonia influences IQ.

The dominantly inherited form is due to a different gene, which requires only one parent carrier who generally has the dystonic symptoms. NINDS studies have shown that persons with this form of dystonia have increased amounts of the enzyme dopamine-beta-hydroxylase (DBH) in the blood.

The third, acquired form of dystonia, is caused by injury, as a result of certain infections, or as a reaction to certain drugs.

NINDS has recently released a fact sheet, *Torsion Dystonia*, describing the symptoms, stages, and treatment of this disease. Science writers can obtain a free copy of this fact sheet by writing: NINDS, NIH Building 31, Room 8A-03, Bethesda, MD 20014.

#

News Releases Issued

RESEARCH AWARDS--Consolidation of existing research training and fellowship authorities of the various components of NIH and the Alcohol, Drug Abuse, and Mental Health Administration into a unified National Research Service Awards Program was announced by HEW Secretary Caspar W. Weinberger. Proposed regulations governing the new program were published on January 17, 1975, in the *Federal Register*. This action was taken in accordance with the responsibility given the HEW Secretary under Title I of Public Law 93-348, the "National Research Act," which was enacted July 12, 1974.

#

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Research Advances

SCIENTISTS DEVELOP NEW GUIDE TO RENAL FAILURE DRUG THERAPY

Three scientists have culled from 472 references what is known about current renal failure therapy with commonly-used drugs, and have compiled a comprehensive guide that can be used to plan such treatment rationally.

Patients with impaired renal function often require major adjustments in dosage of common therapeutic agents to avoid adverse reactions or further renal damage because of reduced or absent renal excretion of these drugs. This exhaustive literature search has now provided a practical guide to pharmacological management of adult patients in this category, particularly those undergoing regular, periodic dialysis.

Drugs are listed in alphabetical order in five tables, either individually by generic name or under subdivisions based on the major type of pharmacologic action. The tables suggest maintenance dosage intervals for common drugs used in patients with renal insufficiency. If information about a specific drug is unavailable, emphasis is given to its biological half-life, normal pharmacology, and creatinine clearance for modification of usual dose schedules.

Maintenance dosage interval recommendations are based on excretion or metabolism of the drug, as well as on the normal biological half-life in hours, and its prolongation with various degrees of renal failure. The qualitative effect of dialysis on drug removal is recorded, as is the type of dialysis employed: hemodialysis, peritoneal dialysis, or both. Nephrotoxic or adverse effects specifically related to renal failure are noted, and adjustments for concurrent dialysis are suggested.

(more)

Renal Failure (Cont'd)

The drug tables are designed to provide the clinician with rough guidelines on which to base safe and effective therapy, but not as a substitute for clinical judgment. The tables will require constant reappraisal to ensure adequate therapy without toxicity, as well as periodic revision to incorporate information about new drugs and newer data about old drugs.

The extensive bibliography is available from the authors: Cecil J. Coggins, M.D., of Massachusetts General Hospital, William M. Bennett, M.D., of the University of Oregon Medical School, and Irwin Singer, M.D., of the University of Pennsylvania School of Medicine. They reported their findings in the *Journal of the American Medical Association*, December 16, 1974. Dr. Coggins is a grantee of the National Institute of Arthritis, Metabolism, and Digestive Diseases.

#

DOWN'S SYNDROME--Every pregnant woman wants a healthy baby. But many women do not know that, with increased age, they face an increased risk of bearing a child with a genetic defect such as mongolism, according to the National Institutes of Health. Mongolism, or Down's syndrome, is one of the most common causes of mental retardation.

#

Research Advances

ELECTRON MICROSCOPY DETECTS FIBERS IN LUNG TISSUE

Researchers indicate that electron microscopy demonstrates an association between submicroscopical asbestos fibers and severe interstitial pulmonary fibrosis. The relationship is not detectable by light microscopy.

Scientists, supported in part by the National Institute of Environmental Health Sciences (NIEHS), used a light microscope to examine lung tissue obtained at open biopsy of a 63-year-old male. The tissue specimen showed severe interstitial fibrosis with no evidence of asbestos bodies. But with the electron microscope, magnification beyond 10,000 times revealed small fibers. At 20,000 to 31,000 times, chrysotile fibers, the most common form of asbestos used in the United States, filled all fields of view. Particles were uniform and minute in size, suggesting the fibrils may have resulted from their fragmentation before they were inhaled or from their degradation *in vivo*. Prior investigations of the relation between the size of respirable mineral particles and the frequence and severity of pulmonary disease have been based on light microscopy; thus, the role of submicroscopical particles was overlooked.

The researchers indicate that submicroscopical asbestos fibers in the lungs are pathogenic and can result in progressive tissue alterations.

They suggest that lung tissue showing alterations and diagnosed as "usual interstitial pneumonia," "fibrosing alveolitis" or "idiopathic pulmonary fibrosis" be examined by electron microscopy.

The investigators--Arthur M. Langer, Ph.D., and Irving J. Selikoff, M.D., grantees of NIEHS; and Albert Miller, M.D., and Alvin S. Teirstein, M.D.--published their findings in *The New England Journal of Medicine*, January 9, 1975.

#

Research Advances

IMMUNE REACTION CLARIFIED IN INFECTIOUS MONONUCLEOSIS

Both T cells and B cells, the two classes of lymphocytes involved in the immune response, increase in number during the acute phase of infectious mononucleosis. This increase occurs without a significant shift in the proportion of one class of white cells to the other. These findings by NIH grantees have helped to clarify events taking place during the clinical course of this acute, common disease of children and young adults, and may lead to the development of ways to prevent or treat the illness.

Infectious mononucleosis (IM) is characterized by fever, sore throat, swollen glands, and an increase in the number of white cells in the blood, including unusual-looking lymphocytes known as Downey cells. Although this increase in lymphocytes has long been recognized in mononucleosis, its significance has not been well understood and there has been a general feeling that, since cellular immunity seems to be depressed in IM, T cells might very well be in short supply.

Using newly developed techniques for distinguishing T cells (thymus-derived) from B cells (bone marrow-derived), scientists at the University of New Mexico School of Medicine compared the numbers of T and B cells in the blood of IM and non IM patients. All samples of sera from the carefully diagnosed IM patients showed increases in lymphocytes shortly after onset of disease with a gradual diminution in numbers as recovery began. T and B cells, however, increased and decreased proportionately within the total population.

Recent reports that the sera of IM patients often contain antibodies reactive with subpopulations of both B and T cells were confirmed by the

(more)

present study; but these antibodies were not, apparently, capable of producing shifts or changes in proportions of circulating T and B cells. Although the temporary depression of T cell immunity associated with IM could not be correlated with any decrease in T cells, the scientists suggest that T cell function may somehow be muted or altered by the lymphocyte-reactive antibodies generated during the course of the disease.

Robert N. Enberg, M.D., Betty J. Eberle, Ph.D., and Ralph C. Williams, Jr., M.D., whose work is supported by the National Institute of Allergy and Infectious Diseases and the National Institute of Arthritis, Metabolism, and Digestive Diseases, reported the results of their research in the August 1974 issue of the *Journal of Infectious Diseases*.

#

DUST ALLERGY--House dust--a nuisance, but harmless to most people--can be a source of troublesome symptoms to others who are sensitive to something in the dust, according to the National Institutes of Health. Those people may be constantly bothered by sneezing and a runny nose, or watery, itchy eyes. Because dust is found virtually everywhere, this allergic reaction knows no season.

#

Research Advances

PROMISING PSORIASIS TREATMENT INVOLVES DRUG, SPECIAL LIGHT

The oral administration of methoxsalen plus exposure to a newly-developed, high-intensity, longwave ultraviolet light system has led to complete clearing of skin lesions in 21 psoriasis patients, according to a Boston scientist whose work is supported by the National Cancer Institute (NCI) and the National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD).

The management of generalized psoriasis, whether by topical or systemic therapy, has not been satisfactory for the two to eight million Americans who suffer from this frustrating and unsightly skin disease. Use of methotrexate, the most effective systemic agent, may be associated with severe liver toxicity, while ultraviolet radiation following local application of crude coal tar requires hospitalization for up to two weeks.

Complete and rapid clearing of generalized psoriasis has now been described in 21 patients following oral administration of a photoactive drug, 8-methoxypsoralen (methoxsalen), and exposure to high-intensity, longwave ultraviolet light. Although these results are preliminary, and maintenance therapy is required in most cases, they could lead to development of a safe and effective ambulatory therapeutic modality for psoriasis.

Sixteen (Group I) of the 21 patients with generalized, refractory psoriasis were treated on one affected side with conventional ultraviolet light, and on the other affected side with longwave ultraviolet light, after ingesting 30-50 mg of methoxsalen. Five patients (Group II) were treated with methoxsalen followed by longwave ultraviolet light only.

(more)

All Group I patients ultimately were switched to longwave ultraviolet light plus methoxsalen when it was noted that this combination treatment was more effective than normal ultraviolet light plus methoxsalen, and complete clearing of psoriatic lesions occurred in all 16 patients. The lesions in five patients in Group II also cleared completely after 12-18 treatment sessions. Subsequently, during a seven month follow-up period, the patients were kept clear of lesions with infrequent outpatient treatments.

Orally administered methoxsalen, which has been used for 20 years in the treatment of vitiligo, was well tolerated by the psoriatic patients. The interaction of light and drug, termed "photochemotherapy" by the investigators, presumably inhibits epidermal DNA synthesis and, thus, retards the well-known rapid local proliferation of psoriatic skin at the lesion sites.

Thomas B. Fitzpatrick, M.D., of Massachusetts General Hospital, working with an NCI research grant and an NIAMDD training grant, and associates reported their study in the *New England Journal of Medicine*, December 5, 1974.

Note to Subscribers

We are aware that this story has received some press attention, but we think it is important to bring these details to all of our subscribers.

#

CATARACT DATA--A cataract is a cloudiness or opacity in the lens which interferes with vision. A cataract is not a film or membrane that grows over the eye, according to the National Institutes of Health.

#

News Feature

NIDR WILL SUPPORT COMMUNITY CARIES PREVENTION PROJECTS

School-based demonstration projects to determine the cost-effectiveness of fluoride mouth rinsing and fluoride dietary supplements to prevent caries will be funded in a limited number of low-fluoride communities by the National Caries Program of the National Institute of Dental Research (NIDR).

Because nearly 50 percent of all children under age 15 have never been to a dentist, school-based projects are viewed as a practical means of reaching children. A recent survey by the American Dental Association showed that most dentists favor this approach to caries prevention.

This program is also responsive to a recent call by the United States Senate that the NIDR engage in more effective dissemination and application of research findings in caries. Through these projects the National Caries Program will demonstrate the feasibility of applying research findings to widespread disease prevention.

Dental schools, local and state health departments, and other interested organizations and institutions have been invited to submit proposals for competitive contract funding.

The projects will be conducted in kindergarten and in grades one through eight. The techniques to be used in the classroom consist of a weekly mouth rinsing with a fluoride solution and the daily use of a fluoride tablet. These procedures are inexpensive, require few materials, are easy to learn, can be readily supervised by non-dental personnel with minimal training, involve little time, and can be carried out without serious interruption of normal classroom activity. NIDR expects to fund 20 to 30 of these caries prevention demonstration projects for a period of 36 to 42 months.

#

Photo Feature

"TRICK" AND "TREAT" GIVEN INTENSIVE CARE

These orangutan twins, born prematurely on Halloween 1974 at Vilas Park Zoo, Madison, were rushed to the Wisconsin Regional Primate Research Center. Because each ape weighed less than two pounds and was having feeding difficulties, they were given intensive care in 90-degree incubators at the Center, which is supported by the NIH Division of Research Resources. The hairy pair, shown at age one month, is now progressing well. The Halloween fraternal twins are "Trick" (right), a male, and his sister "Treat." *(NIH Photo #1352)*

#

News Feature

SLE PRODUCES CHANGES IN CONNECTIVE TISSUE

Systemic lupus erythematosus (SLE) is an uncommon disease of connective tissue. It produces changes in the structure and functions of the skin, joints, and internal organs.

There is evidence suggesting that the disease may be the result of a disorder in the body's production of "antibodies," special protein substances used by the body in defense against bacteria and other foreign invaders. In SLE, abnormal antibodies are produced which may go awry and react with the patient's own body tissue.

The disease is found most often in persons 15-30 years of age (usually women), but it has been observed in all age groups. SLE may begin with any number and combination of symptoms. Frequently the skin is affected. Sometimes a facial rash takes the form of an open butterfly, spread over the bridge of the nose and cheeks. Other notable features of SLE include weakness, lack of energy, loss of appetite, and loss of weight. The patient may develop anemia, and may have a low white blood cell count. Infections are frequent and were a common cause of death in SLE before the advent of antibiotics.

The number and variety of symptoms of SLE are great. The disease may begin in any organ or system. In many cases, it is a mild nonprogressive disease. In others, the episodes of active disease may be short-lived, or arrested by therapy, and the patient remains completely well for long periods. Frequently, such patients suffer no recurrence of symptoms.

(more)

SLE (Cont'd)

The cause of SLE is not known, therefore there is no specific and complete treatment for the disease. SLE varies from person to person, both in its symptoms and its response to treatment, and is often difficult to diagnose. The drugs most effective against it may themselves cause serious side effects. Recent clinical and basic research, however, have considerably broadened medicine's choice of treatment weapons.

The treatment of SLE must be tailored to fit the specific case. When the skin is affected, exposure to the sun should be avoided. The general measures of supportive care, including relief of pain and maintenance of good nutrition, are essential. Sufficient rest is important, especially during periods when the disease is most active.

Specific therapy must be given for any complications, such as infections, which may develop during the course of the disease. Beyond these general measures, antimalarial and anti-inflammatory drugs have been effective in many cases. Aspirin, the most conservative of the anti-inflammatory agents, has often proved effective.

Steroid hormones are effective in suppressing most of the disease activity, but the dangers of prolonged treatment with these drugs in a chronic disease are great. Strict medical supervision is required. At present, research is under way to determine the value in SLE of some drugs which interfere with the body's ability to produce antibodies.

The National Institute of Arthritis, Metabolism, and Digestive Diseases conducts research in SLE, as well as supporting SLE research programs at various institutions through the Nation.

#

Photo Feature

ACTIVATED FORMS OF VITAMIN D CAN BE USED TO TREAT DISEASES

An investigation of the function of Vitamin D has led to the discovery that it must be converted in the body to activated forms. In 1968, Professor Hector F. DeLuca, a biochemist at the University of Wisconsin-Madison, and his colleagues isolated the first activated form of vitamin D_3 which was called 25-HCC. In 1971, he and his group isolated a still more active form called 1,25-DHCC. They chemically synthesized these compounds and an important analog la-hydroxy vitamin D_3 to make them available for clinical application.

These activated forms of vitamin D are now being used successfully in the treatment of bone diseases that previously were very difficult to manage. Although patients with kidney failure cannot make the $1,25\text{-}(OH)_2D_3$, they can be successfully treated with this compound and its analog $1aOH\text{-}D_3$. Patients who do not possess their parathyroids also fail to synthesize $1,25\text{-}(OH)_2D_3$ when it is needed to mobilize calcium. They, too, can be treated successfully with the $1,25\text{-}(OH)_2D_3$.

Research into the function and uses of the various new forms of vitamin D_3 in the treatment of certain diseases has been supported by the National Institute of Arthritis, Metabolism, and Digestive Diseases.

Dr. DeLuca's discovery is an example of how basic research can lead to a rewarding practical application. Basic research in biological sciences is designed to seek information on how living things work. In this case the data has led to new and promising ways of treating bone disease.

(more)

Vitamin D (Cont'd)

Dr. DeLuca is shown studying vitamin D in his laboratories at the University of Wisconsin-Madison. His research is supported in part by the National Institute of Arthritis, Metabolism, and Digestive Diseases. (NIH Photo #1353)

#

News Feature

AGED RATS AND MICE ARE AVAILABLE FOR RESEARCH

Aged rats and mice from three to 24+ months old are available under certain conditions from the National Institute of Child Health and Human Development (NICHD).

The NICHD Adult Development and Aging Branch maintains under commercial contract a colony of aged inbred Fischer 344 rats and C57BL/6, BALB/c and CBF_1 (F_1 hybrid cross of C57BL/6 x BALB/c) inbred mice for research on aging.

The animals may be provided to investigators now doing aging research, or for pilot studies in anticipation of later submission of a research grant application on aging. The aged rats and mice are caesarean originated and maintained behind a barrier system to exclude microbial pathogens. Characterization data including life tables, growth curves, organ weights, age-associated pathology, and blood chemistries are available on the Fischer rat, and are now under acquisition in the mouse strains.

Investigators interested in acquiring animals from the colony should submit a detailed request. If the scientist is not currently supported by this Branch, additional information must be submitted.

Since the contract is partially self-sustaining, reimbursement at the rate of $2.60 per month of age for the rats and $.60 per month of age for the mice may be required. Some animals may be provided to investigators for pilot studies in lieu of reimbursement if it is determined that the data developed from the study may be relevant to the Branch's program in aging research.

(more)

Requests for aged rats and mice should be directed to Don C. Gibson, D.V.M., NICHD, Landow Building, Room A709, Bethesda, MD 20014 or telephone: (301) 496-1033. This activity will soon be transferred to the recently-established National Institute on Aging.

#

CANCER WEAPON--The best weapon against cancer still is early diagnosis, according to the National Institutes of Health. Half of all cancers start in parts of the body that can be examined easily by a doctor during an ordinary office visit. Prompt treatment by qualified physicians offers the greatest hope.

HODGKIN'S DISEASE--The National Institutes of Health uses a special four-drug combination treatment for patients with Hodgkin's disease. Of every 100 patients so treated, 80 went into complete remission; 65 of the 100 can expect to remain alive, and 40 will be continuously free of disease after five years.

FERTILITY--The current decline in fertility in many countries is due to sharply lower fertility rates at the older childbearing ages (over 25), according to the National Institutes of Health.

#

New Publication:
Voluntary Health Agencies Working to Combat Neurological and Sensory Disorders

The National Institute of Neurological Diseases and Stroke (NINDS) actively cooperates with the voluntary agencies dealing with neurological, sensory, and communicative fields.

NINDS has released a new publication, *Voluntary Health Agencies Working to Combat Neurological and Sensory Disorders*, which lists the agencies, officers, and addresses.

Science writers can obtain a copy of this publication from:

NINDS
Bldg. 31, Room 8A-03
National Institutes of Health
Bethesda, MD 20014

#

News Releases Issued

CORONARY DRUGS--Drugs that reduce blood levels of certain fatty substances--notably cholesterol and triglyceride--apparently do not confer any protection against recurrent heart attacks or improve long-term survival among men who have previously experienced one or more acute heart attacks. This is according to findings reported from the National Heart and Lung Institute's Coronary Drug Project.

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Research Advances

"Symbolic Overlay"...

NIDR HOLDS WORKSHOP ON ORAL-FACIAL PAIN

A stoic may say, "Doctor, I hate to bother you, but I have an annoying pain. It's not too bad, but I guess I ought to do something about it." Then he will describe his pain as "pounding, shooting, and cramping." A more excitable patient may say, "Doc, you gotta help me. I can't stand this unbearable pain. It flickers, jumps, and pinches me." Whose pain is more severe? Information and ideas discussed at a recent Workshop on Oral-Facial Pain, sponsored by the National Institute of Dental Research (NIDR), should help doctors answer this question by enabling them to evaluate pain more effectively, regardless of individual and cultural differences.

In addition to the incalculable costs of suffering, chronic pain costs billions of dollars annually in medical expenses and loss of working time, according to John J. Bonica, M.D., who presided at the November 1974 workshop in Bethesda. Dr. Bonica, chief of the Department of Anesthesiology, University of Washington School of Medicine, Seattle, added that pain in the face and head regions is likely to have "a special symbolic overlay" that pain elsewhere rarely causes.

Even though much pain is of mixed or unknown origin, more than 25 experts in various dental, medical, and psychological aspects of pain were asked at the workshop to subdivide oral-facial pain into four major categories: vascular, musculoskeletal, neurological, and psychological. For each of these categories, a subcommittee identified and described information needed to diagnose and treat conditions causing that type of pain.

(more)

In addition, preliminary agreement was sought on standardizing the terminology now used to describe various pain conditions in order to dispel some of the confusion that now hinders the comparison of research findings. General acceptance of standard terms would improve the collection and retrieval of pain data and thus permit currently impossible studies of the epidemiology and treatment of oral-facial pain. At present, data are not available on the incidence of the various pain syndromes.

Although pain is usually considered only as a symptom, Dr. Bonica observed that severe, chronic pain can become a disease state which must be treated as such over long periods. Indeed, pain sometimes outlasts the pathology that originally caused it. An example is phantom-limb pain which an individual experiences in a limb that no longer exists.

Management of pain is complicated by the fact that some people claim great relief from a placebo (a pill that contains no active drug), while others are unrelieved by any medication. Other psychological contributions to pain situations exist and must be treated by psychological means.

Ronald Melzack, M.D., of McGill University, Montreal, reported a means of evaluating pain using approximately 100 words that patients have employed to describe and evaluate pain. By focusing on 20 key words from this master list, Dr. Melzack can derive a pain-rating index which enables him to correct under- or over-estimates of pain that patients from different cultural backgrounds tend to make.

Usually when a patient receives the list of pain-describing adjectives, he is delighted that "now I can tell exactly how it feels. Before, I couldn't

think of just the right words." Dr. Melzack reports that pains described as flickering, jumping, and pinching are less severe than those termed pounding, shooting, or cramping. So even when stoics or cancer patients--who often minimize their pain and make light of their suffering--complain, the sensory words they use to describe it not only tell what kind of a pain it is, but also indirectly indicate how much pain is felt.

Physiological pain cues were discussed by Richard A. Sternback, M.D., director of the Pain Unit of the Veterans' Administration Hospital, San Diego. In patients with acute pain, the signs of increased heart rate, blood pressure, sweating, and muscle tension all indicate a response of the autonomic nervous system to anxiety. He finds that tranquilizers and muscle relaxants bring relief to many of these patients.

Most of these signs are absent in chronic pain which is characterized by loss of appetite, interest, libido, and a change of sleep patterns. Since some depression occurs in all cases of chronic pain, Dr. Sternback said, drugs which relieve depression may help such people, but relaxants do not. Management of chronic pain often requires the coordinated efforts of a team to evaluate the physical findings, results of laboratory tests, activity charts kept by patients themselves, reports from social workers, drug records, and psychological information.

Dr. Sternback also reported that recent biochemical studies suggest that pain and depression may have a common metabolic pathway. Some doctors have found that supplying a patient with some of the neuroamines which are depleted by serotonin during depression sometimes relieves both his depression and his pain.

(more)

Pain (Cont'd)

Dr. Sternback urged doctors to consult psychologists about the use of diagnostic tests for psychological problems to be sure that a patient has such problems, before he automatically refers a patient to a psychologist because no physical cause of pain has been discovered.

Frederick W.L. Kerr, M.D., a neurologist at the Mayo Clinic, Rochester, classified the origin of all pain as neuropathic, non-neuropathic, or unknown. "Pain due to clinically demonstrable dysfunction or to observable pathology of a peripheral nerve is a neuropathy," he said. In other known types of pain, healthy nerves carry pain messages which may arise in the central nervous system, or be of vascular, musculoskeletal, psychologic, or unknown origin. Also his sub-committee recommended that the suffix "-algia" be used to indicate pain, and suggested that words that end in "-itis" be limited to descriptions of clinical inflammation.

In the final session, workshop participants dealt with some of the problems of computer-assisted collection, storage, and retrieval of information essential for evaluation of the overall pain problem, and for planning future research needs and directions.

NIDR hopes to publish the findings of this workshop as a guide to further pain research, especially in the clinical area.

#

BREAST CANCER--The National Institutes of Health wants to make breast cancer screening more widely available throughout the country. In a joint program with the American Cancer Society, several breast cancer detection clinics are open where women can receive thorough examinations without charge.

#

Research Advances

NIH SCIENTISTS IDENTIFY ORIGIN OF MALIGNANT CELLS

The origin of malignant white blood cells can now be identified by NIH scientists using markers on the cells' surfaces. Their findings should lead to a new classification of human lymphoid tumors, thereby improving the diagnosis and prognosis of patients with such disorders.

Malignant lymphoid cells preserve many characteristics of "normal" immune response cells--the T cells (thymus-derived lymphocytes), B cells (bone marrow-derived lymphocytes), and monocytes. The presence or absence of these characteristics can be used to identify cell populations.

Using several techniques (including their own) which identify receptors on normal cells, National Institute of Allergy and Infectious Diseases (NIAID) and National Cancer Institute (NCI) researchers studied malignant cells either in suspension or in extremely thin slices of frozen tissue. These abnormal, malignant cells were from patients with lymphomas (tumors) of uncertain cellular origin, such as "hairy cell leukemia" and histiocytic medullary reticulosis.

These two conditions were found to be monocyte proliferations; while poorly differentiated lymphoma and Mycosis Fungoides were determined to be T cell disorders. Abnormal cells of Sezary Syndrome patients also exhibited T cell characteristics, including the production of MIF--a chemical generated by sensitized lymphocytes when they interact with antigen. This finding confirms the belief of many scientists that Sezary Syndrome and Mycosis Fungoides--both lymphomas with malignant involvement of the skin--are closely related. Identification of T cell origin should enable accurate diagnosis

(more)

of Sezary Syndrome, which has often been confused with chronic lymphocytic leukemia, a B cell disorder.

The NIH scientists hope that determination of the precise origin of lymphoma cells will provide insights into the factors that cause the tumors. In addition, the ability of these tumors to produce large uniform populations of monocytes or T or B cells will provide researchers with valuable tools for further studies of both normal and malignant immune response cells. Abnormal T cells could also be used to isolate human T cell lymphokines--chemical mediators of cellular immunity. Overproduction of such mediators may be the cause of the "boiled lobster" appearance of the skin of Sezary Syndrome patients.

The researchers caution, however, that these techniques are still in their infancy and need refinement. The chemical nature and precise mode of action of the cell receptors is completely unknown. Future studies will determine whether receptors on normal cells are really identical to those on malignant cells.

Ira Green, M.D., Ethan M. Shevach, M.D., and Michael Frank, M.D., of NIAID and Elaine S. Jaffe, M.D., Richard L. Edelson, M.D., and Costan W. Berard, M.D., of NCI presented their findings at the International Academy of Pathology meeting in 1974. Their report will appear in the Academy's journal.

#

HYPERTENSION--Twenty-three million Americans have high blood pressure and half of these are not aware they have the disease. Left uncontrolled, high blood pressure leads to heart failure, stroke, and kidney disease, according to the National Institutes of Health.

#

Research Advances

RENAL STONES TREATED WITH DIPHOSPHONATE

In preliminary clinical trials, orally-administered diphosphonate (EHDP) inhibited the basic calcium phosphate renal stone formation process without adverse effects and, so, may have prophylactic value in chronic stone formers.

The investigators reported in 1973 that disodium ethane-1-hydroxy-1, 1-diphosphonate (EHDP), when added to urine *in vitro*, inhibits the growth and nucleation of burshite, a calcium phosphate salt with a special crystalline configuration which forms the basis for certain renal stones. It had been shown earlier that orally administered EHDP is excreted unaltered in the urine. These findings led to the present clinical trial of EHDP in patients with calcareous renal stones.

Oral administration of EHDP for one to six months in eight patients with absorptive hypercalciuria and renal stones has resulted in marked inhibition of crystal growth of brushite, as well as in inhibition of brushite nucleation, without significant side effects. It is suggested that EHDP may be clinically useful in preventing formation of renal stones of calcium phosphate origin.

The eight patients were hospitalized in a metabolic ward for six to seven days before and after one, three, and six months of EHDP therapy. Urine samples were obtained periodically and analysed for crystal growth inhibition, calcium, phosphorus and cyclic AMP. Periodic blood samples were analysed for calcium, phosphorus and alkaline phosphatase, and the intestinal absorption of calcium and "bone density" were measured.

(more)

Renal Stones (Cont'd)

EHDP's ability to inhibit crystal growth of brushite was dose-related, being insignificant at 5 mg/kg/day* and becoming appreciably greater at 20 than at 10 mg/kg/day*. In three patients there also was inhibition of nucleation of brushite. A positive correlation between crystal growth inhibition of brushite and urinary concentration of EHDP was noted. Five patients who passed 34 stones in three years before EHDP therapy passed only four stones during one year of such treatment.

Except for a transient rise in serum alkaline phosphatase activity and a slight increase in urinary cyclic AMP, no significant side effects were encountered. Intestinal calcium absorption and bone density did not change significantly. More extensive clinical study and evaluation of its potential toxicity is needed to determine EHDP's ultimate efficacy in prophylaxis of nephrolithiasis.

Charles Y.C. Pak, M.D., and Masahiro Ohata, M.D., of the University of Texas Southwestern Medical School, Dallas, reported their study in *Metabolism*, Vol. 23, No. 12.

Dr. Pak is a grantee of the National Institute of Arthritis, Metabolism, and Digestive Diseases.

*milligrams per kilogram of body weight per day

Note to Subscribers

We are aware that this story has received some press attention, but we think it is important to bring these details to all of our subscribers.

#

Research Advances

Background Report...

NCI ANNOUNCES ISOLATION OF A VIRUS FROM LAB-GROWN HUMAN LEUKEMIC CELLS

National Cancer Institute (NCI) scientists have reported the isolation of a virus from the laboratory-grown leukemic cells of a 61-year-old woman with acute myelogenous leukemia.

The scientists have not yet determined whether the human virus causes acute myelogenous or other leukemias in man. Acute myelogenous leukemia, as well as other forms of cancer, may be caused in an unknown fashion by combinations of external and hereditary factors. However, the scientists have demonstrated the biochemical and immunologic similarity of the human virus to two viruses that cause cancer in primates other than man. One of these viruses causes myelogenous leukemia in the gibbon ape, a close relative of man; the other causes solid tumors in woolly monkeys.

Myelogenous leukemias are cancers of the blood in which precursor cells in the bone marrow fail to mature properly into normal white blood cells. The disease primarily affects adults and is extremely difficult to treat effectively. Acute myelogenous leukemia is a rare form of cancer, occurring in about two of every 100,000 persons in the U.S. each year.

The characteristics of the virus, as determined so far, clearly indicate that it was derived from the human cells. The virus has a core of RNA (ribonucleic acid) and the characteristics of a family of viruses known as type-C. Viruses of this type can cause cancer in a wide variety of animals.

Isolation of the virus provides scientists for the first time with a human virus that may be useful in identifying the one or more factors that

(more)

cause acute myelogenous leukemia. The virus also may enable scientists to develop new approaches to detection, diagnosis, and treatment of human leukemias.

Robert E. Gallagher, M.D., and Robert C. Gallo, M.D., of NCI's Laboratory of Tumor Cell Biology, Division of Cancer Treatment, reported their findings at the annual meeting of the American Society of Hematology in Atlanta in December 1974. The scientific paper describing isolation of the virus appeared in the January 31, 1975 issue of *Science*. S. Zaki Salahuddin, of Litton Bionetics, Inc., assisted in the study. The team is supported by the NCI Virus Cancer Program in collaboration with the Division of Cancer Treatment.

The NCI team isolated the human virus three times from different test-tube cultures of the patient's cells. A blood sample drawn from the patient at the M.D. Anderson Hospital and Tumor Institute, Houston, Texas, by Ken McCredie, M.D., was sent to NCI where Dr. Gallo and his coworkers divided the leukemic cells into seven test tubes for frozen storage and attempts to grow the cells in laboratory cultures.

Using various cell culture methods, the scientists mixed the patient's cells in the test tube with growth fluid supplemented with fluid from laboratory-grown human embryonic cells. They found that the fluid from the embryonic cells contained a "factor" believed to be a protein, that was essential for growth of the leukemic cells.

After a minimum of five weeks in culture, the leukemic cells began to produce a virus with a core of RNA and the characteristic appearance of the

(more)

type-C virus. Drs. Gallagher and Gallo then conducted extensive studies of the internal components of the human virus to rule out the possibility of contamination by animal cancer viruses.

They found that the biochemical and immunologic properties of the internal components of the human virus were distinct from those of known animal cancer viruses, although the human virus was remarkably similar to two type-C viruses that cause cancer in non-human primates. In addition, they found that fresh, uncultured leukemic cells from the same patient contained viral components with the same properties as the internal components of the virus in the patient's laboratory-grown cells.

As early as 1970, Dr. Gallo and other coworkers detected in human acute leukemic cells an enzyme resembling reverse transcriptase, a cancer-virus associated enzyme. Since that time, the scientists have purified the reverse transcriptase and the RNA in the cells. The scientists extensively characterized these internal components and demonstrated their similarity to the RNA and reverse transcriptase of cancer viruses from the gibbon ape and woolly monkey.

The scientists indicated that they will concentrate next on determining whether occurrence of the human virus is limited to one patient or one type of leukemia, or whether the virus is found in a wider range of patients and leukemias. They also will study whether leukemic patients have antibody to the virus or its proteins in their blood and whether the antibodies are present at only one point or during the course of the disease. Antibodies are produced by the body's immune system when stimulated by foreign microorganisms or other agents.

(more)

At the same time, the NCI team will work to determine whether the virus produces a protein on the surface of leukemic cells. Such a protein, if isolated and injected into laboratory animals such as rabbits, might provide antibody preparations that could be examined for their ability to destroy leukemic cells growing in the test tube. If such a technique were successful, the antibody might be useful in destroying residual cancer in treated leukemic patients.

Antibodies to the virus or to leukemic cell components produced by the virus might have other uses in detection or diagnosis of acute myelogenous leukemia. A test for early detection might be developed if the virus or related components appear prior to present indicators of the disease. Similar tests might be valuable during treatment and follow-up to monitor effectiveness of drugs in destroying leukemic cells.

By studying cell alterations caused by the virus, the scientists also may determine whether the human virus causes damage to white blood cells and whether these changes are permanent.

The weight of epidemiologic evidence indicates that cancer is not a contagious disease in humans, transmitted either by coughing, sneezing, or other contact with a cancer patient. The random pattern of the disease and the apparently long latent period before development of cancer suggest that many factors contribute to susceptibility. Hereditary factors and environmental effects that probably include viruses must interplay in a complex process not yet understood.

#

Photo Feature

ROLE OF PLATELETPHERESIS IN PATIENT CARE IS EXPANDING

The relatively new technique of plateletpheresis permits the transfusion of this blood fraction to patients who have platelet-deficiency disorders.

The plateletpheresis process involves drawing blood from a healthy donor and removing platelets. The remainder of the blood (white and red blood cells and plasma) is immediately returned to the donor. The procedure is repeated four times with the entire process taking from two to three hours.

The donor suffers no physical threat because of the platelet donation since a healthy individual's platelets are replaced within 36 to 48 hours.

Platelets, the smallest cellular components of blood, are necessary for coagulation (or clotting). Without sufficient platelets, patients may suffer severe hemorrhage or fatal bleeding episodes.

A new plateletpheresis program at the NIH Clinical Center is helping to extend the lives of patients with blood disorders such as leukemia, aplastic anemia, and certain other malignant diseases.

At NIH, a community-wide effort to supply specially-matched platelets to patients was started in April 1974. In the first six months 1,172 blood samples were tested. Nearly 500 donors gave platelets through the program, and 1,350 procedures were performed.

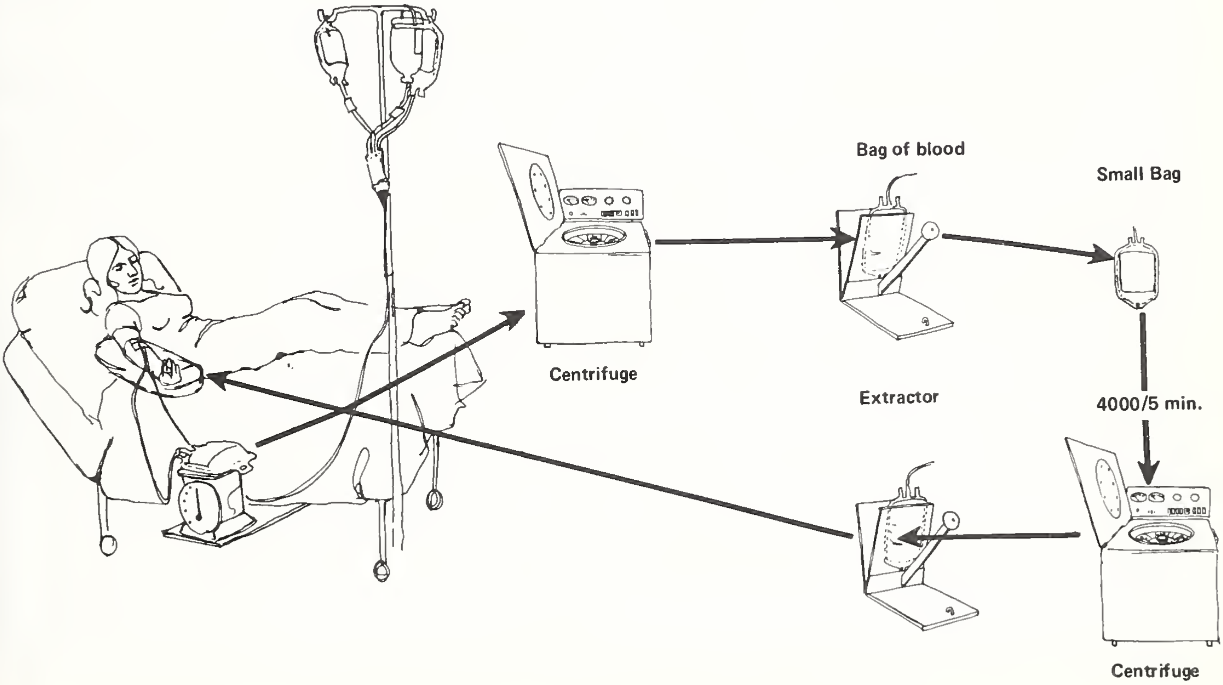
Similarly, most major medical centers and cancer centers are exploring the feasibility of using matched platelet transfusions. With NIH funding, seven medical centers now have matched donor lists tied together by computers. This system provides the capability for exchanging platelets among centers,

(more)

thereby increasing donor pool size for participating centers.

Platelet matching for compatibility between donor and recipient is much more difficult to achieve than that for red blood cell groups. The odds of finding a perfect match between two unrelated individuals is only one in 4,725. So, once a match is found, a donor is likely to be called on several times to give platelets to a patient.

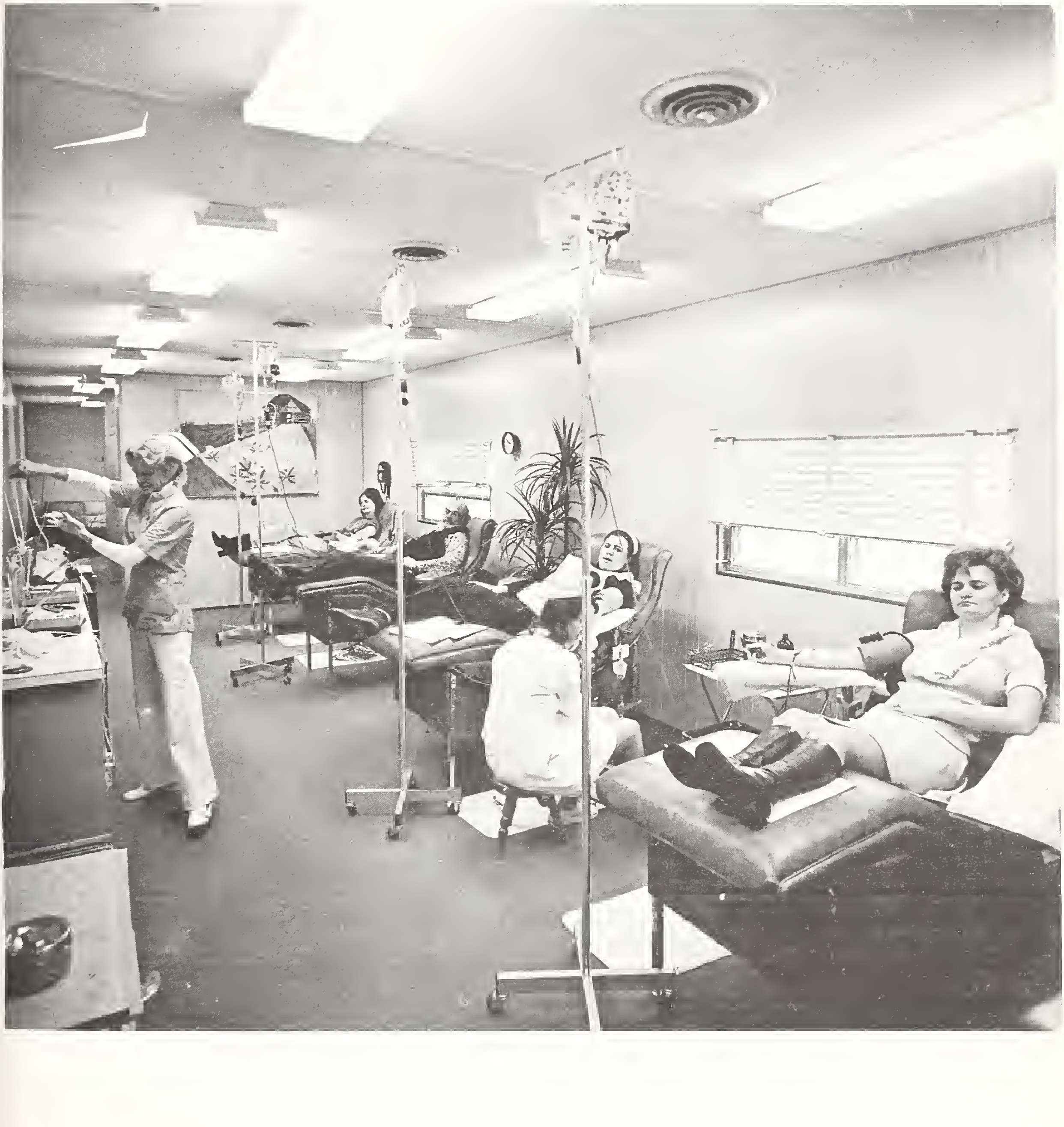
Platelet transfusions have greatly reduced life threatening hemorrhage in cancer patients and other patients with defective bone marrow function.



In the plateletpheresis process, whole blood is taken from the donor, platelets are removed by a technique requiring two centrifugations, and the rest of the blood is returned to the donor. (NIH Photo #1354)

(more)

Plateletpheresis (Cont'd)



The process takes about 150 minutes, with the major "ill effect," boredom, alleviated by color television. A donor receives the platelet-free blood back. The body will replace the platelets within 36 to 48 hours, and then the person will again be eligible to donate either whole blood or platelets. (NIH Photo #1355)

#

News Feature

Improving Surgical Success...

SOFT CONTACT LENSES ARE USED IN TREATMENT OF BURNED EYES

University of Florida, Gainesville, ophthalmologists are improving the treatment of chemically burned eyes by applying soft contact lenses immediately following transplantation of the cornea.

The use of soft lenses is improving surgical success by protecting the transplanted cornea and helping it remain clear, and is improving the restoration of vision in some patients. Visual results vary with severity of the chemical burns and with the presence or absence of other complicating diseases.

Chemical burns of the cornea and front portion of the eye are among the most difficult corneal conditions to treat, and physicians generally have found that alkali burns are more resistant to treatment than acid burns. Corneal transplants performed on these patients have failed in the majority of cases because of graft reactions, such as development of vessels in the corneal tissue, and poor wound healing.

In 1972, the University of Florida physicians began using soft lenses as an adjunct to corneal transplantation. They found that the soft lens (high in water content and non-abrasive to the eye) helped protect the grafted tissue from drying and from irritation by the eyelids.

Among 15 patients treated by the combination of corneal transplantation and soft contact lenses, 10 were reported successful. Success means that none of these grafts opacified (clouding and obscuring vision); vessels did not invade the grafts, and the patients experienced improved vision 10 to 12

(more)

months following surgery. Among the 10 patients, visual acuity was improved from the restricted ability to count fingers or to perceive light to the range of between 20/30 and 20/200. There was a higher success rate among patients with acid burns than with alkali burns (88 percent compared with 71 percent).

Prior to use of soft lenses as an adjunct to transplantation, the University ophthalmologists said they experienced the same high failure rate reported by other clinical teams of treatment of chemically burned eyes via the standard corneal transplantation procedure. Among an earlier group of 16 patients suffering with severe chemical burns who underwent corneal transplantation at the University's Shands Teaching Hospital between 1968 and 1972 there were 13 failures.

"Many factors were analyzed during the care of the total study group of 31 patients, and it appears that application of the bandage soft contact lens has a major influence on the outcome of corneal transplantation for chemically burned eyes," reports Herbert E. Kaufman, M.D. He adds that other factors play important roles in success of treatment including the use of donor corneal tissue with good surface epithelial tissue attachment, the use of very fine surgical thread, regular use of steroids to suppress inflammation and graft reaction, smaller grafts of corneal tissue, and careful post-operative care.

Dr. Kaufman notes that most of the patients in both groups (before and after introduction of soft lenses) had complicating diseases of the eye in addition to chemical burns, and many had undergone previous sight-preserving

(more)

operations. Because of this, Dr. Kaufman said, successes might be higher in patients whose problems were restricted to chemical burns of the eye without other complicating difficulties. Dr. Kaufman is professor and chairman of the University's Department of Ophthalmology.

The study, which involved a critical review of patients referred to the Shands Teaching Hospital for treatment of chemically burned eyes, was supported in part by the National Eye Institute.

#

AMNIOCENTESIS--Amniocentesis was first developed in the latter part of the last century. It consists of obtaining amniotic fluid through the insertion of a needle into the amniotic cavity, according to the National Institutes of Health.

TRANSPLANTS--Kidney transplants were sporadically attempted for almost 40 years before the first successful transplant was accomplished between identical twins, according to the National Institutes of Health.

#

March 10, 1975

Photo Feature

SEATTLE MAINTAINS CENTRAL PRIMATOLOGY REFERENCE FILES

The Primate Information Center (PIC) in Seattle is recognized internationally as the central source for published material on nonhuman primates. It possesses the most extensive primatology reference files in the United States, and possibly in the world.

The information center, located at the Washington Regional Primate Research Center, reviews articles in journals from all over the world, and informs scientists working with nonhuman primates about the publications. Headed by Ms. Maryeva W. Terry, PIC was established in 1963, and is supported by the Division of Research Resources.

PIC offers researchers two types of computer searches. One, a retrospective bibliography, gives a listing of all articles in the file relating to a scientist's question. PIC answers over 900 requests a year for retrospective bibliographies.

For a recurrent bibliography, the scientist tells PIC what his long-term interest is, and once every two weeks the question is checked against recent additions to the computer file.

PIC started with a file of 5,000 citations published since 1939, and now contains over 35,000 references.

PIC issues *Current Primate References*, a weekly which lists citations in all fields of primate research and, if known, the author's address. The publication is circulated to over 1,600 investigators, professors, and graduate students in 50 countries.

(more)

Primatology (Cont'd)

Russia maintains a service similar to PIC at the Institute of Experimental Pathology and Therapy in Sukhumi. The Soviet center, which receives *Current Primate References*, contributes Soviet articles on primatology to the publication.

Two literature analysts discuss the contents of a paper to be added to the Primate Information Center bibliography files. Over 35,000 nonhuman primate references are currently contained in the computerized information system at Seattle. Shown are Julia Polczynski (left) and Benella B. Caminiti. (NIH Photo #1356)

#

News Feature

Meniere's Disease...

SCIENTISTS EXPLORE INNER EAR DISORDER

Meniere's disease is a disorder of the inner ear (which contains the organ for hearing and for balance) characterized by the episodic occurrence of a triad of symptoms--vertigo (dizziness), transient hearing loss, and tinnitus (ringing in the ears).

Although it can occur at any age, it appears most commonly in persons in their 40s and 50s, somewhat more frequently in men than in women. Meniere's disease can be primary, occurring in persons without a previous ear disorder, or secondary, superimposed or as a consequence of some other disorder. In some patients, particularly those whose Meniere's symptoms can be attributed to a definite cause, drugs or surgery may be effective. However, in many patients, particularly those whose Meniere's disease is of unknown origin, the symptoms may become so severe that the patient is unable to continue working or completing everyday tasks.

The duration of Meniere's attacks is highly variable, occurring anywhere from twice a month to twice a year, and lasting from 20 minutes to 24 hours. In addition to the agony of vertigo, tinnitus, and hearing loss during an attack, the patient may also experience nausea, vomiting, and nystagmus (uncontrolled to and fro movements of the eyes).

Meniere's is a prolonged disease which gradually abates as deafness increases. Attacks may spontaneously disappear, or they may continually recur for years.

(more)

Meniere's Disease (Cont'd)

The National Institute of Neurological Diseases and Stroke is supporting basic research to determine the causes of Meniere's disease. Until Meniere's can be prevented, the Institute is also continuing to support research on improved methods of medical and surgical treatment to relieve symptoms.

Research has indicated that the underlying cause of Meniere's disease is an abnormal buildup of fluid (endolymph) in a part of the inner ear (labyrinth) known as the endolymphatic sac. Results of laboratory experiments using thorium, a radioactive tracer, show that it is likely that cell debris from damaged or dying cells is part of the normal cell turnover. However, these cells are not enveloped and consumed in the inner ear by special cells, known as phagocytes. Rather, they are transported to the inner structure called the endolymphatic sac for excretion. If this sac is malfunctioning, the cell debris accumulates into groups (macromolecules) that are too large to be diffused (passed out of the sac through its membrane). This causes an increased osmotic pressure in the sac (more fluid passes into the sac than flows out of it), so that the sac's membrane becomes distended. This distension, or possible rupture of the membrane allowing fluid to flow out, interferes with two other inner ear structures, the cochlea (organ of hearing) and the vestibule (concerned with balance and equilibrium).

Meniere's disease therefore falls into two general types--cochlear or vestibular--depending on which of these two structures is primarily disturbed. As can be expected, the main problem for patients with cochlear Meniere's disease will be hearing, while the predominate problem for those with vestibular Meniere's disease will be balance.

(more)

Meniere's Disease (Cont'd)

In instances where a specific cause of Meniere's symptoms can be found, appropriate drugs may be effective. In fact, it is estimated that approximately 80 percent of persons with Meniere's symptoms can be helped to some degree in this way.

For persons with Meniere's disease of unknown origin, however, the situation is more bleak. Psychotherapeutic drugs, such as Valium, often help alleviate vertigo which is usually the most devastating symptom. But these drugs do not cure the disease or arrest its occurrence. At the present time there are no drugs which can alleviate the symptoms of tinnitus, although scientists are continuing the search.

Surgery is becoming increasingly safe and effective in combating Meniere's disease and is becoming an alternative in patients who cannot be adequately helped by drugs. There are three types of surgery: decompression (drainage) of the endolymphatic sac to re-establish normal inner ear fluid pressures; severing (denervating) inner ear nerves; or destruction of the inner ear structures when hearing is already extremely poor.

Recent advances in electron microscopy have enabled research scientists to gain a better understanding of the physiological basis of Meniere's disease. While Meniere's symptoms produced by secondary causes now often can be cured, symptoms of Meniere's disease of unknown origin have been much more difficult to treat. Scientists at all levels are continuing to explore the possible methods of preventing Meniere's disease, and of curing it either medically or surgically so that its victims may be restored to a normal life.

#

New Publication:
The National Institutes of Health Associateship Program

Training opportunities for young physicians anticipating research careers are described in a new NIH publication, *The National Institutes of Health Associateship Program.*

The full color leaflet provides general information about the two- to three-year associateships at NIH.

Applications are currently being accepted for appointments beginning July 1977 and later. There are a few openings for 1976. Candidates may apply during their third or fourth year of medical school or during internship or residency. Most enter the program following one year of residency.

Application deadline is April 18, 1975. Interviews will be conducted by invitation at NIH June 16 through 27. Travel will be paid by NIH. Selections will be made in July by a matching process similar to the National Intern and Residency Program.

Copies of the associateship leaflet, a 1975 program catalog, and application forms are available by writing or calling collect: The Associate Director, Clinical Center, National Institutes of Health, Bethesda, Maryland 20014; telephone (301) 496-2167.

#

News Releases Issued

CANCER STUDY--The National Cancer Institute has awarded contracts totaling $1.5 million for a study of vaginal cancer and other noncancerous genital tract irregularities in offspring of mothers who received synthetic estrogens during pregnancy. The information obtained in the study should form the basis for advising affected offspring of the risk of developing some abnormality. The proper management for any such abnormalities may also be suggested by the study.

PAIN DRUG--Nitrogylcerin, a drug in use for more than 100 years to relieve the chest pain of angina pectoris, may also be effective in reducing the extent of heart-muscle damage resulting from acute heart attacks, and in reducing the threat of heart-rhythm disturbances that are a frequent consequence of such attacks. These disturbances sometimes lead to the patient's death, according to the National Heart and Lung Institute.

DIABETES CENTER--A fifth Diabetes-Endocrinology Center will be established by the National Institute of Arthritis, Metabolism, and Digestive Diseases to expand ongoing fundamental and clinical research efforts on this metabolic problem. The newest Center will be at the Washington University, St. Louis. The Center concept is designed to foster a collaborative approach to research, and to facilitate project coordination among investigators where a significant diabetes research program already exists.

#

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Phone: (301) 496-1206

Research Advances

NIH SCIENTISTS DEVELOP NEW MEANS FOR FILMING CELLULAR PHENOMENON

Scientists at NIH have developed a unique electro-optical system which has enabled them to observe and record, for the first time, the invasion of red blood cells by malaria parasites. As reported in the February 28, 1975, issue of *Science*, this system--which can be applied to other areas of biomedical research--has helped to clarify the crucial sequence of events by which the organism causing malaria begins its life cycle in the blood.

Malaria continues to rank as one of the major killers of mankind, especially children. More than one billion people live in endemic areas, and half of these people live in locales where there are no efforts to control the spread of the parasite. Knowledge gained through advances such as this system could one day facilitate the prevention of malaria by interrupting the invasion of the red blood cells by the malaria parasite.

The NIH group--James A. Dvorak, Ph.D., Louis H. Miller, M.D., and Tsugiye Shiroishi of the National Institute of Allergy and Infectious Diseases' Laboratory of Parasitic Diseases, and Willard D. Whitehouse of the Clinical Center's Television Engineering Section--have discovered, through use of their new system, the manner in which the merozoites, a form of the malaria parasite, enter normal red blood cells. Only the merozoite's anterior end--containing minute structures, the paired organelles--is capable of attaching to the red blood cell.

Initial attachment of the parasite to the red blood cell results in rapid and marked deformation of the red blood cell for 10 to 15 seconds. Then, the merozoite enters the cell by producing a localized infolding of the cell

(more)

Electro-Optical System (Cont'd)

membrane. Complete invasion of the red blood cell requires approximately 10 to 20 seconds.

The Bethesda group believes that the merozoite produces a hole in the red blood cell membrane which is later sealed off. After a second deformation wave that accompanies actual entry of the merozoite, the red blood cell resumes its normal shape and serves as a host for the development of the malaria parasite.

To record these rapidly occurring events, the researchers had to develop a system that would overcome the technical problems which, until now, had prevented this study from being performed.

The initial problem--keeping the live cells in a normal state while being observed with a microscope--was solved by using a special controlled environment culture chamber invented by Dr. Dvorak and Woodrow Stotler in 1971. This chamber was fitted to a microscope equipped with optics that eliminated the problem normally associated with observing living red blood cells.

Attached to the microscope was a high sensitivity television camera which transmitted the "live" action to electronic equipment that recorded high resolution images. Maintenance of this high degree of resolution was the concern of the researchers throughout the project. Selected television segments were further processed with special electronic equipment to produce a 16 mm motion picture.

The scientists decided to use the television system because the low light level required to prevent damage to the red blood cells and parasites

(more)

provided only 1/1000 to 1/10,000 the amount of light required for the fastest available motion picture film. The television system also permits detailed analysis of individual images throughout the entire sequence of events by studying the film on video tape.

A film, "The Invasion of Erythrocytes by Malaria Merozoites," depicting all of the events described in the *Science* report, may be obtained from the National Medical Audio Visual Center in Atlanta.

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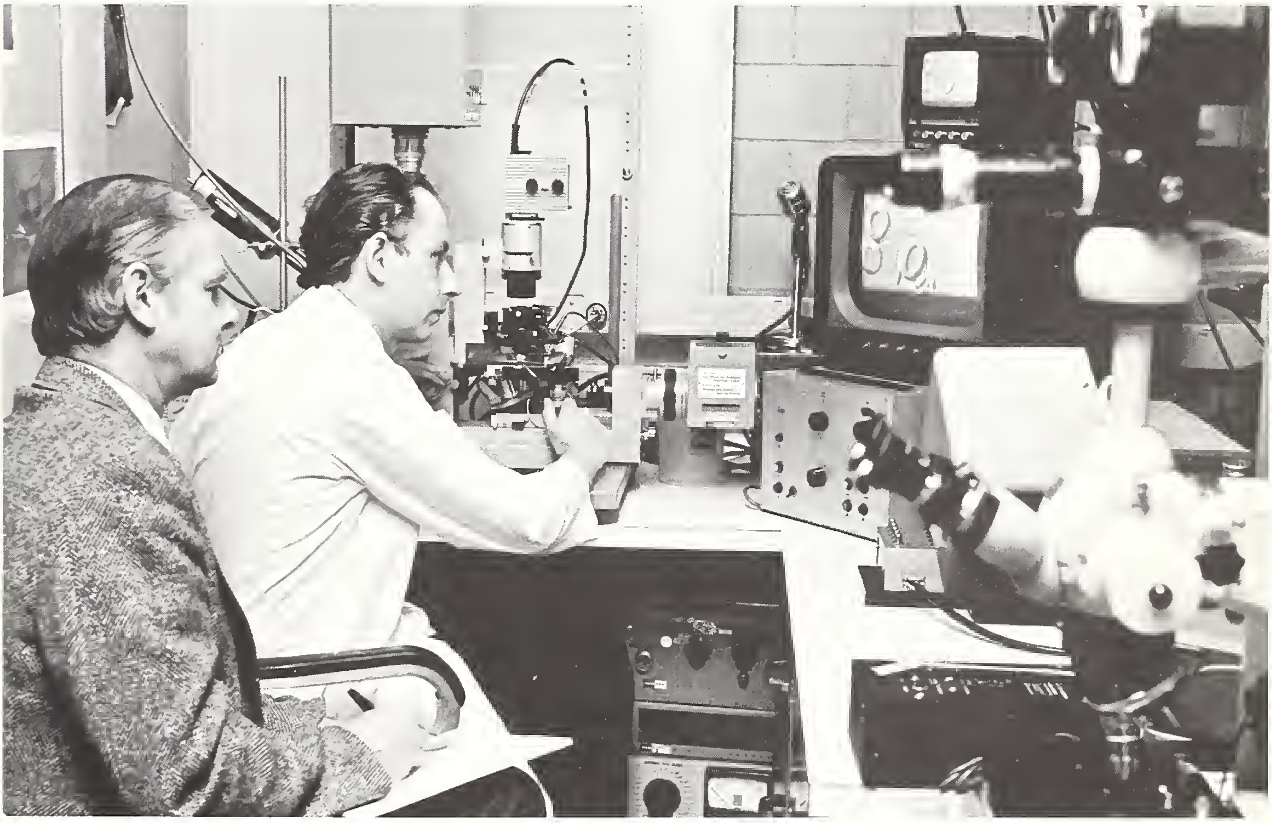
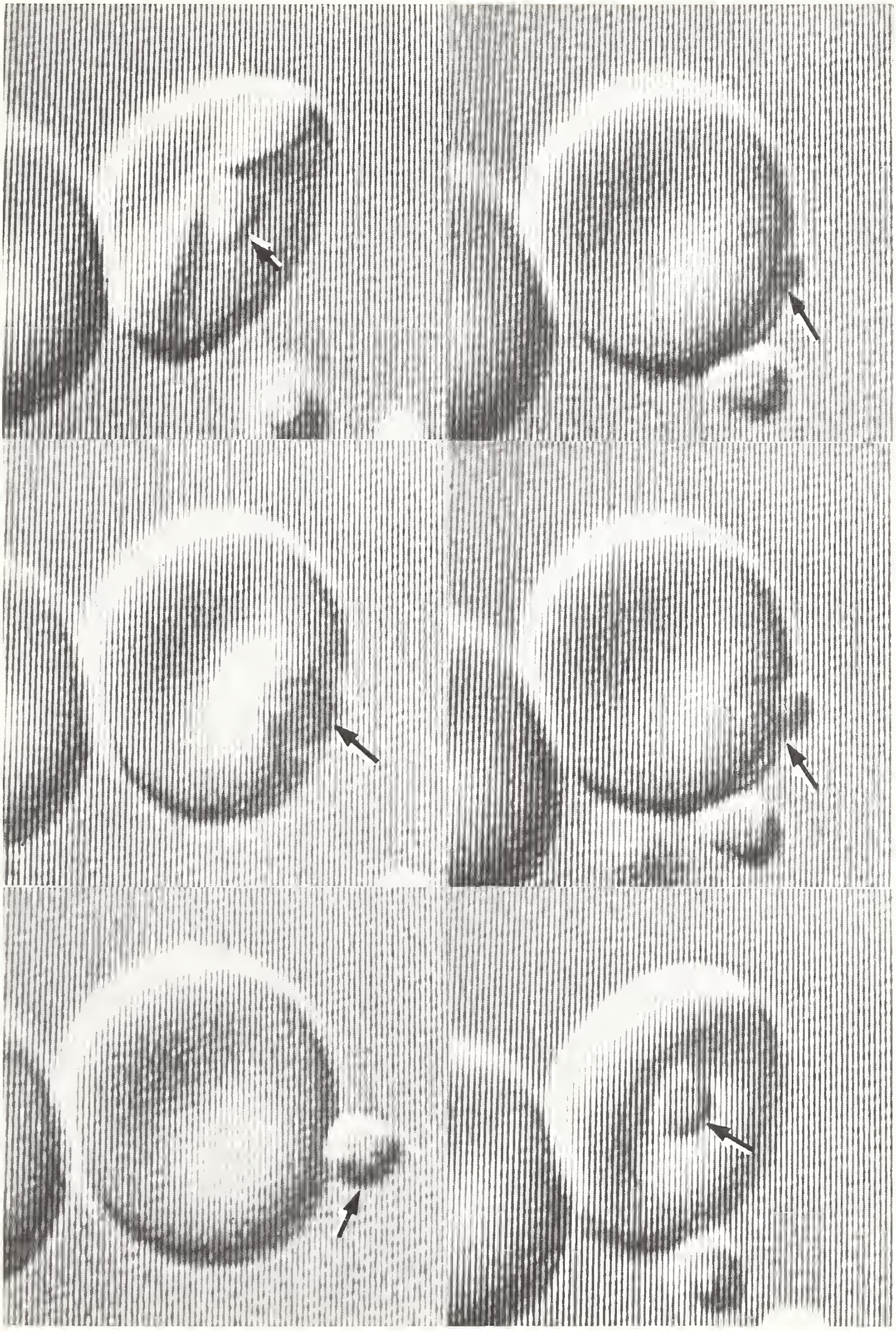


Willard Whitehouse (left) of the NIH Clinical Center's Television Engineering Section, and James A. Dvorak, Ph.D., of NIAID's Laboratory of Parasitic Diseases, view the invasion of red blood cells by malaria parasites on their television monitor. A television camera attached to the microscope picks up the "live" action which is then recorded on video tape. Special electronic equipment is then used to process selected television segments and produce a 16 mm motion picture film. (NIH Photo #1357)

Electro-Optical System (Cont'd)



This inverted microscope sequence shows (from upper left to lower right) the invasion of a red blood cell by a malaria parasite (arrow). Following attachment of the parasite to the red blood cell, there is a marked distortion of the red blood cell followed by the relatively slow invasion of the red blood cell by the parasite. (NIH Photo #1358)

#

Research Advances

During Cancer Treatment...

SPECIAL DIET MIGHT EASE INTESTINAL COMPLICATIONS

A special diet may be effective in managing severe intestinal complications that result from radiation treatment in children with cancer.

The new work in radiation enteritis (inflammation of the intestine) was done by Sarah Donaldson, M.D., at Stanford University Medical School, while she was a visiting fellow at the Institut Gustave-Roussy in Villejuif, France. She recently described the work at a meeting of the American Society of Therapeutic Radiologists.

Dr. Donaldson and her colleagues studied 44 children in France who had received whole abdominal irradiation as part of the management of their malignant disease. It was determined that subsequent inflammation of the intestines and bowel obstruction in these children was caused by the radiation, not by recurrence of the tumors.

The problem may be life-threatening, even though the cancer has been arrested. According to Dr. Donaldson, "No specific dietary therapy has been developed for this condition in children."

The diet consists of a blended mixture of substances that can be taken through a tube if the patient is too sick to eat or drink it. It is free of gluten (the protein of wheat and other grains), free of protein obtained from cow's milk and lactose, low in fat, and low in residue.

Dr. Donaldson calls it a "diet by omission," since it was developed by eliminating all the food items that affected the enteritis.

(more)

Diet (Cont'd)

"Our work under the microscope gave us the clues," she says. "We made it free of fat and milk products, since we saw that the damaged bowel could not absorb milk. We made it low residue to avoid further obstruction."

Dr. Donaldson describes a "dramatic reversal in the children's clinical status that began with the initiation of the diet."

Followup for the 14 long-term survivors ranged between 19 months and seven years. There were no deaths attributed to radiation enteritis. Of those surviving, none has shown evidence of recurrent intestinal obstruction.

Roughage, gluten, milk, and fat were gradually added to the children's diets following improvement in their X-rays and small bowel biopsies. The diet, continued for 12 to 24 months in some cases, was gradually replaced to a normal diet which was well-tolerated.

The paper is the first description of the syndrome of intestinal injury following whole abdominal radiation in childhood. Dr. Donaldson points out that as the survival rate of children with these tumors increases, such complications of treatment become more apparent.

This is also the first time a specific dietary therapy has been published as the major form of treatment for radiation enteritis in children. Work is now underway at the Institut Gustave-Roussy to determine if use of the diet during the period of radiation treatments would avoid later intestinal complications. The diet is not yet in use at Stanford, but is under study.

The research was supported in part by grants from the National Cancer Institute.

#

Research Advances

NIDR Grantees...

INVESTIGATORS SEARCH FOR OBJECTIVE TEST FOR PAIN

Seattle scientists have reported an objective way to measure and record brain responses to specific, painful, electrical stimulation of the pulp of human teeth.

The method overcomes some stumbling blocks to scientific studies of pain. First is the previous impossibility of measuring pain perception objectively. Second is the difficulty of separating pain messages to the brain from other sensations such as pressure or temperature.

Gian Emilio Chatrian, M.D., and his associates at the University of Washington, have added to other studies which have shown that the small nerve fibers in tooth pulp function almost exclusively in conducting painful stimuli to the brain, and have developed a method of delivering electrical impulses of a known strength, duration, and wave form to selected teeth. To accommodate the electrodes they drill two holes into the dentin where minute tubules give the current access to the pulp. After completion of the tests, the holes are filled.

The investigators then place electrodes at various positions on the surface of the head to pick up those brain waves that occur in response to series of short, moderately painful impulses to the teeth. The scientists use a computer to extract these wave patterns and distinguish them from other coincidental electrical activities of the brain which tend to mask them. The clearest patterns come from electrodes placed at the top and at the center of both sides of the head.

(more)

The scientists recorded consistent and reproducible pain patterns among themselves and normal volunteers. In one instance they found no patterns when they stimulated a tooth from which the pulp had been removed. Another living tooth in the same person gave normal pain patterns. A man, who had never felt pain of any kind because of a defect in his nervous system, gave a flat, waveless, response to electrical stimulation similar to that from the dead tooth. This is believed to be due to the congenital absence of small, pain-carrying nerve fibers. Autopsy of the man's brother, who had also felt no pain, revealed such a lack. In normal volunteers, the anesthetic mepivacaine also abolished the brain wave responses to pain.

In other parts of the body, pain messages cannot be separated from other types of information to the brain as clearly as in tooth pulp. Therefore, the scientists plan to use the technique described above to study the effectiveness of various pain-relieving drugs as well as other procedures said to alleviate pain such as acupuncture, hypnosis, and stimulation of peripheral nerves.

This research, which was supported in part by the National Institute of Dental Research, has been reported by Dr. Chatrian, Donald F. Farrell, M.D., Robert C. Canfield, D.D.S., Ettore Lettich, REEGT, in *Archives of Neurology*, in press; by Drs. Chatrian, Canfield, Lettich, and Richard G. Black, M.D., in the *Journal of Dental Research*, September-October 1974; and Drs. Chatrian, Canfield, Lettich, and Thomas A. Knauss, M.D., at the 28th annual meeting of the American Electroencephalographic Society, July 25, 1974, in Seattle.

#

Research Advances

NIH EVALUATES DRUGS FOR LUPUS NEPHRITIS

Two NIH scientists have shown, in a double-blind controlled study, that cyclophosphamide is superior to azathioprine in the short-term treatment of lupus nephritis.

There is no satisfactory form of therapy for lupus nephritis, a grave kidney disorder associated with systemic lupus erythematosus (SLE). In 1971, the investigators showed that the cytotoxic and immunosuppressive drug cyclophosphamide is superior to placebo in the short-term treatment of lupus nephritis. In the present study they have compared the relative efficacy of two such drugs, cyclophosphamide and azathioprine, and of placebo in the treatment of such patients over a longer period of 10 weeks.

Cyclophosphamide was found to be significantly superior to both azathioprine and placebo in the treatment of lupus nephritis, while azathioprine was not significantly better than placebo in any individual measure. Although cyclophosphamide led to somewhat greater improvement than did azathioprine, additional long-term data will be required to establish the role of these potent immunosuppressive drugs in the routine management of lupus nephritis.

The 38 patients hospitalized with lupus nephritis were randomly assigned to receive either cyclophosphamide, azathioprine, or placebo, and were permitted to have up to 0.5 mg per kg per day of prednisone for extrarenal manifestations of their underlying disease, SLE. Renal function, urine sediment, proteinuria, anti-DNA antibodies, the third component of complement (C3), and clinical symptoms were assessed during a two-week control period

(more)

and after a 10-week treatment period.

Cyclophosphamide was significantly superior to both azathioprine and to placebo for all six measures together and for the three renal measures alone. It also was significantly better than placebo with regard to proteinuria, urinary RBC, and serum C3. Azathioprine was significantly better than placebo when all six measures were considered, but was not significantly better in any individual measure.

Although the mechanism of action of cyclophosphamide and azathioprine in the treatment of lupus nephritis is as yet unknown, there is considerable evidence to indicate that cyclophosphamide and prednisone, in particular, act together well. Ongoing long-term studies of the described patients, designed to obtain long-term data on the relative efficacy of cyclophosphamide and azathioprine, may provide more insight into their mechanism of action.

Alfred D. Steinberg, M.D., and John L. Decker, M.D., of the National Institute of Arthritis, Metabolism, and Digestive Diseases reported their findings in *Arthritis and Rheumatism,* December 1974.

#

MYASTHENIA GRAVIS THERAPY--During the past two decades, scientists have reported significant reductions in mortality and morbidity from myasthenia gravis, a neuromuscular disease characterized by weakness and abnormal fatigue of the voluntary muscles. This success is due in part to the work of the National Institute of Neurological Diseases and Stroke's myasthenia gravis research program.

#

Research Advances

CLINICAL COMPARISON MADE OF DENTAL RESTORATIVE MATERIALS

Some Emory University investigators have compared the clinical performance of composite resin, silicate, and amalgam filling materials in the four most common types of tooth restorations.

A traditional amalgam (New True Dentalloy) was the standard for gauging the performance of composite preparations in molars of the same individual. In 34 sets of Class I restorations (those placed in the chewing surfaces of molars and surrounded completely by enamel) the amalgam retained its anatomic form better than Addent (a glass-filled composite resin) or Adaptic (a quartz-filled composite resin) over a four-year observation period. However, both composites maintained better adaptation to the margin of the cavity than the amalgam after three years. Recurrent decay was not a problem with any of the materials.

In 43 pairs of matched Class II restorations, (two or more surfaces of a molar tooth repaired by each filling) the comparison was between Adaptic and amalgam over a three-year span. Again, recurrent decay was no problem, the plastic surpassed in marginal adaptation, and the amalgam in anatomic form.

In Class II, IV, and V restorations of anterior teeth, Adaptic was compared with a silicate cement (M.Q. Silicate). Composites and silicates are preferred for anterior restorations because their color matches that of enamel better. Class III findings are placed in surfaces where teeth adjoin; Class IV are used to restore the angles of incisors; and Class V repair surfaces that face either the tongue or the lips. Forty-three pairs of these anterior restorations were available for study over a three-year period.

(more)

No decay recurred in any of these restorations. At the end of the observation period, the composite fillings had maintained their color as well as the silicates and were consistently superior in marginal adaptation and anatomic form. Moreover, although they developed some surface irregularities, the silicates developed more.

In this entire series of clinical observations, none of the materials developed clinically significant fractures, as expected. Observations of matched pairs of restorations over longer periods will be necessary to establish the limits of durability for composites. The durability of silicates is known to be less than that of amalgams.

These findings were reported in the *Journal of the American Dental Association* in November 1974 by Wilmer B. Eames, D.D.S., R. Terrell Weitman, D.D.S., Jon D. Strain, D.D.S., and Alfred K. Williams, D.D.S. The work was supported by the National Institute of Dental Research.

#

SEVERE FACIAL PAIN--Severe facial pain, often accompanied by jaw clicking and limited jaw movement, is as puzzling to dentists and physicians as it is to its sufferers. Now, a University of Illinois Medical Center team, aided by a National Institute of Dental Research grant, has evolved a theory explaining the cause of the condition myofacial pain-dysfunction syndrome. When there is no pathology in the joint hinging the jaw to the skull, pain generally comes from habitual tooth grinding and clenching in response to stress. Such oral habits produce muscle spasms, wear away cusps on the grinding surfaces of teeth, and even can force teeth out of alignment.

#

Research Advances

Hormone Studies...

SOMATOSTATIN MAY DECREASE BLOOD GLUCOSE IN DIABETICS

A San Francisco scientist has shown that the hypothalamic hormone, somatostatin, acutely decreases blood glucose levels in diabetic patients, presumably by inhibiting glucagon secretion, and thus may prove useful in the management of diabetes.

In 1971 a grantee of the National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD) reported that diabetes is characterized by excessive glucagon secretion, in addition to insulin deficiency, and thus may be a bihormonal disorder. (Glucagon, a hormone secreted by pancreatic alpha cells, stimulates the release of glucose from liver glycogen stores and tends to elevate blood glucose levels.) More recently, the present investigators demonstrated that infusion of the hypothalamic "growth hormone inhibiting factor" somatostatin into normal human subjects results in a lowering of plasma glucagon and glucose levels.

The investigators now have shown that infusion of somatostatin into diabetic patients decreases plasma glucagon levels by 50 percent and plasma glucose levels by 25 percent. Moreover, somatostatin combined with insulin was more effective than insulin alone in diminishing postprandial hyperglycemia, and it is suggested that this hypothalamic hormone, in some longer-acting form, may be a useful adjunct to insulin in the treatment of diabetes.

To evaluate the role of glucagon in the hyperglycemia of diabetes, 1 mg of somatostatin was infused over a two-hour period into 10 fasted, insulin-dependent diabetic patients, and its effect on plasma glucagon and glucose

(more)

levels was determined. Additional studies were conducted to determine the relative effects of somatostatin and insulin on plasma glucose changes after a meal.

Plasma glucagon levels fell from 150 to 77pg/ml and plasma glucose levels from 260 to 191 mg/100 ml. Similar responses were seen in a hypophysectomized diabetic patient, indicating that somatostatin's effects were not due to growth hormone inhibition but were probably due to a direct inhibition of glucagon secretion by the pancreas. Somatostatin infusion, together with subcutaneous insulin administration, completely abolished postprandial hyperglycemia and was more effective than subcutaneous insulin alone.

These findings indicate that excessive glucagon secretion accounts for about 25 percent of the fasting plasma glucose levels in insulin-dependent diabetic patients. Somatostatin's hypoglycemic effect is probably due to decreased glycogenolysis and hepatic release of glucose caused by suppression of endogenous glucagon secretion.

Peter H. Forsham, M.D., of the University of California, San Francisco, and associates reported their study in the *New England Journal of Medicine*, September 12, 1974. This research was supported in part by NIAMDD.

#

PARAPLEGIA--Each year, spinal cord injuries add an estimated 5,000 to 10,000 new persons to the Nation's more than 100,000 paraplegics. Many programs initiated by the National Institute of Neurological Diseases and Stroke are aimed at reducing these statistics.

#

Photo Feature

Still Experimental...

MEDICAL PION GENERATOR IS PROMISING NEW CANCER TOOL

Stanford University scientists have developed a promising new tool for cancer treatment, and will soon begin testing it in living cells and laboratory animals. Called a medical pion generator, the new tool will use a stream of pimesons, subatomic particles generated by a high-energy accelerator, to kill cancer cells with miniature nuclear explosions.

It will take three to five years before the treatment is available to patients, but if pion beam therapy becomes a reality, it could mark a milestone in cancer radiotherapy.

It would enable physicians to attack more successfully some cancers now difficult to treat. These include cancers of the mouth and throat, certain tumors of the brain and lungs, or those which presently go untreated because they are resistant to conventional radiation.

The pion generator is the result of work by Malcolm Bagshaw, M.D., Henry S. Kaplan, M.D., H. Alan Schwettman, Ph.D., Douglas Boyd, Ph.D., and William Fairbank, Ph.D. The five men have worked for nearly four years to bring the pion generator to this stage of development.

Stanford's team is one of four groups in the U.S., Canada, and Europe exploring the potentialities of pion therapy today. At least two others are expected to begin treating patients ahead of Stanford, but Stanford's represents the only effort to develop a machine which could be installed in a hospital, where it will serve the maximum number of patients.

(more)

The Stanford researchers announced their development at a two-day conference on technical aspects of pion radiotherapy and future clinical applications in January 1975.

Pions (also known as pimesons) are small particles found in the nuclei of atoms. They make up the "glue" or "cement" that holds protons and neutrons together in the nuclei. Pions can be generated by the newest, most powerful high-energy particle accelerators of the type used in nuclear research. When pions strike living tissue, they slow down and are eventually captured by nuclei in atoms of living cells. A nucleus which captures a pion explodes. This miniature nuclear explosion is known as "star formation."

"Because," Dr. Bagshaw explains, "the nuclear fragments produced in this explosion cause such great destruction, pion therapy is expected to be about three times as effective in killing tumor cells as X-rays giving a comparable radiation dose."

Furthermore, pions can be stopped quite precisely in a target region by varying their momentum. Thus, tissue damage can be confined entirely to the tumor volume. X-rays, on the other hand, are attenuated gradually and many pass through the body, damaging healthy as well as malignant tissue.

Another advantage of pions is that the radiation released during the miniature atomic explosion within the cells can be detected, and therapists expect to see exactly where cell destruction is taking place.

Finally, the Stanford medical pion generator involves a radical new approach for delivering cancer-killing radiation which should further improve treatment with little or no damage to nearby healthy organs or other tissue.

(more)

Work on the pion generator, the scientists said, has also spawned three new instruments essential to the pion system. They were developed by Dr. Boyd in the High Energy Physics Laboratory. One instrument measures the density of tissues that pions must enter. This is important because knowing the density, radiotherapists will then be able to adjust the momentum of the pions so that they will stop and be captured at the exact location of the tumor.

A second instrument will be used to monitor the actual pion stopping region during treatment. When pions are captured in the tumor and explode, they give off gamma rays which can be detected. With this type of information, radiotherapists can be sure that every day's treatment utilizes a stopping region which coincides with the location of the tumor. A third instrument developed by Dr. Boyd will be used to pinpoint the location of the tumor itself.

The treatment approach grew out of the way Drs. Schwettman and Fairbank designed the pion generator. "It really opened the way to a new kind of dose distribution in the patient," said Dr. Kaplan.

The Stanford pion generator was designed and built in the High Energy Physics Laboratory with approximately $1 million in grants from the Research Applied to National Needs program of the National Science Foundation. The planned experiments with living cells and laboratory animals will be supported with new funding from the National Cancer Institute.

If medical pion generators like the current prototype are installed in a hospital, four could be operated off a single accelerator. Such an

(more)

accelerator for hospital use has not yet been built. For testing purposes, the present pion generator is energized by a relatively large and expensive accelerator constructed originally for physics research.

But the scientists are confident that once the pion therapy is proven superior to conventional radiotherapy, a scaled-down version that would fit into a hospital could be constructed.

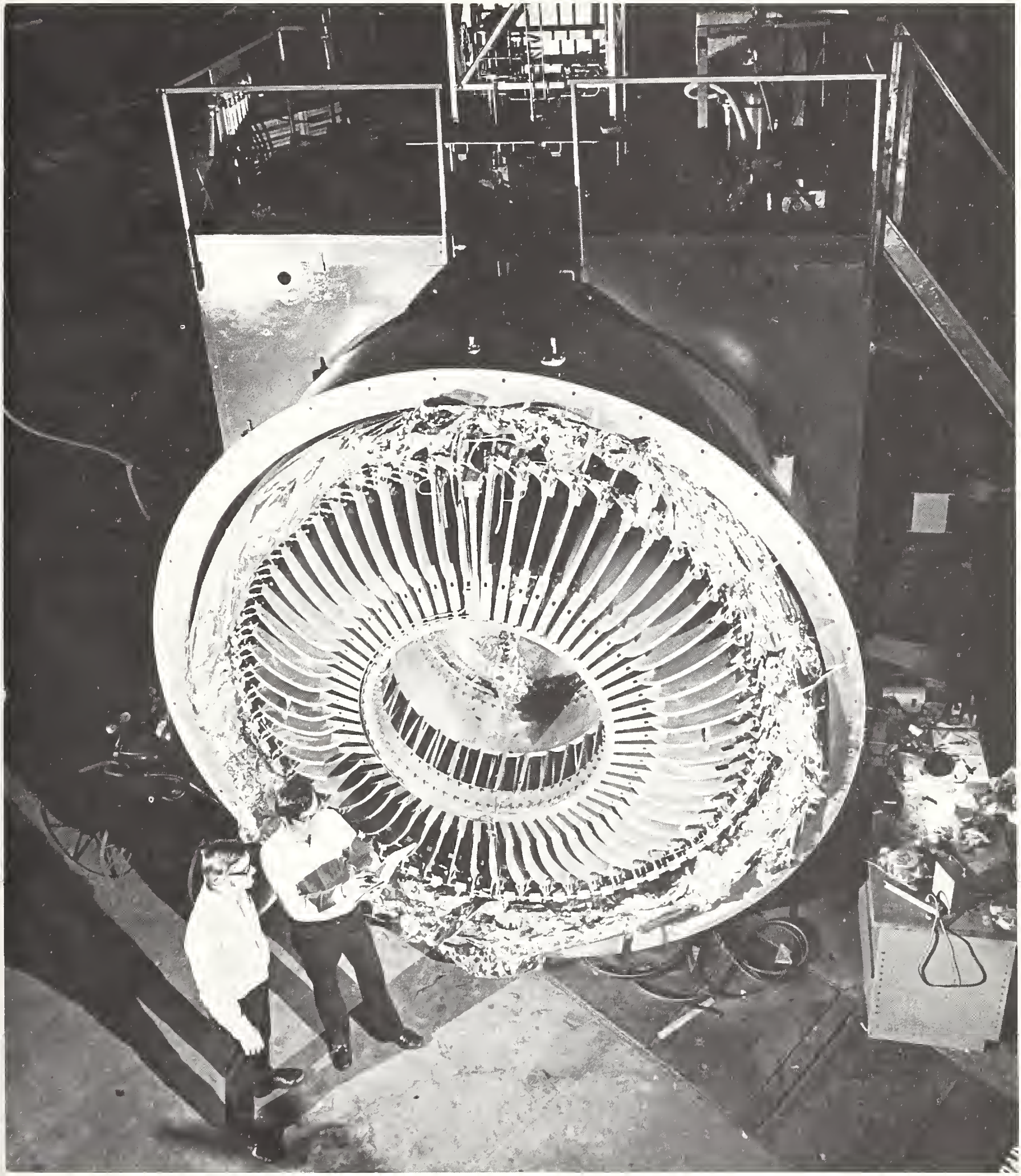
The accelerator, four pion generators, other equipment and the building might cost about $8 to $10 million at today's prices, which is comparable to building and equipping a radiotherapy facility in a large medical center, the scientists said.

Dr. Fairbank feels the medical pion generator should make radiotherapy much more like surgery. Not only will cancer therapists have a much better "knife" at their disposal--but for the first time they will really have "eyes" to see where it is cutting.

The interior (see photo on page 19) of the Stanford medical pion generator is made up of 60 individual magnet coils placed like photo slides in a slide tray. The magnets will collect subatomic particles called pions as they emerge from a target and direct them to the patient. Standing by the pion machine are Douglas Boyd, Ph.D., and H. Alan Schwettman, Ph.D., of the High Energy Physics Laboratory. The machine will undergo testing for the next three to five years before it is used for cancer treatment in patients. (NIH Photo #1359)

(more)

Pion Generator (Cont'd)



(See caption on page 18.)

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News Feature

DIABETIC NONHUMAN PRIMATES SERVE AS RESEARCH MODELS

Scientists at the Oregon Regional Primate Research Center are studying the occurrence of spontaneous diabetes in nonhuman primates to better understand the illness in man.

The work is headed by Charles F. Howard, Jr., Ph.D. It was Dr. Howard who first developed a technique for inducing diabetes mellitus in pig-tailed macaques. He also was the first researcher to discover spontaneous diabetes in the Celebes apes at the Center, which is supported by the Division of Research Resources.

The incidence of the disease in humans is between two and three percent of the population. Through intensified study, researchers at the Center indicate that one percent of the nonhuman primates--apes, monkeys, prosimians--may be affected. Because of some similarity in how spontaneous diabetes affects both species, the animals serve as excellent models for research of the disease. For example, there is some evidence that the diabetic nonhuman primates are predisposed to environmental stress, particularly diet. Scientists, hoping to draw an analogy between diabetes in man and his nonhuman counterpart, conjecture that human diabetes may also be a unique result of man's inability to cope metabolically with his environment.

Secondary complications--atherosclerosis, muscle microangiopathies, and cataracts--that develop in the animals are also analogous to the human complications.

Atherosclerosis, a deposition of fatty substances in the arteries, is a major threat to human diabetics often resulting in a higher than normal rate

(more)

of heart attacks and cardiovascular disease.

Previously, in order for scientists to study the disease, it was necessary to induce the condition in animals by feeding them a high fat diet. But in spontaneous diabetic Celebes apes, the disease develops even without high fat diets, thus enhancing the value of the primate as a research model.

Muscle microangiopathies is a condition in human diabetics causing the basal lamina of the capillaries to thicken, inhibiting the passage of nutrients and oxygen. A form of tissue starvation results which can eventually develop into a gangrenous state. Nonhuman primates are generally less severely afflicted than man, but researchers at the Center diagnosed muscle microangiopathies in a Sykes monkey--the first time a case was reported in an animal model.

Prolonged diabetes can also result in the appearance of cataracts, a clouding of the lens of the eye. Ophthalmologists performed cataract surgery on the black Celebes ape and the pig-tailed macaque resulting in sufficient sight restoration.

The Oregon Regional Primate Research Center houses many diabetic animals--rhesus and squirrel monkeys, pig-tailed and crab-eating macaques, prosimians, and bushbabies. All serve as valuable models for determining the cause of diabetes, breeding desired normal and diabetic characteristics, and elucidating how the secondary complications of diabetes can be prevented.

#

News Feature

Hereditary Illness...

HUNTINGTON'S DISEASE HAS PHYSICAL, MENTAL SYMPTOMS

Huntington's disease is an hereditary disorder characterized by a combination of physical and mental symptoms, either of which may appear first. Often, however, the physical symptoms come first, and usually between the ages of 35 and 40, by which time the individual may have passed the disorder on to several children.

Early symptoms may be confused with fidgety nervousness. The uncontrollable chorea (series of movements) may show itself as jerking, twisting, and spasms of the muscles of the face, tongue, neck, trunk, arms, and legs. As symptoms become more severe the patient may have trouble swallowing and may be unable to speak.

Huntington's disease also may begin with distressing personality changes, such as indifference, dullness, irritability, poor judgment, loss of memory, and carelessness about personal looks and habits. Outbursts of violence may occur, alternating with periods of short-lived depression. In later stages the patient may become profoundly demented.

Huntington's disease is passed on through an autosomal dominant gene, which means that each offspring of an affected person has a 50 percent risk of having the disease. Males and females of any ethnic groups may be affected.

If a person does not show symptoms by age 35, the probability of his having the disease diminishes with each succeeding year. In very rare instances, however, individuals over 70 years old have been known to develop the Huntington's disease symptoms.

(more)

Because of its hereditary nature and categorization as a "mental" disease, families have hidden its existence for centuries and it is almost impossible to assess accurately statistics regarding the prevalence of Huntington's disease in the United States.

A review of a number of studies on the prevalence of Huntington's disease in various world populations indicates a fairly uniform distribution which would mean that about 10,000 to 14,000 Americans have Huntington's disease symptoms. However, since the establishment of the voluntary organization called the Committee to Combat Huntington's Disease (CCHD), incoming letters, phone calls, and personal contacts have led the CCHD to believe that three to four times this number may have the Huntington's disease gene. They either have Huntington's disease symptoms or will eventually develop symptoms.

There is, as yet, no means to test and identify persons with Huntington's disease before symptoms become apparent. The diagnosis of Huntington's disease is usually based on the clinical findings of dementia, and chorea, and positive family history. The insidious onset of involuntary movements is unlike most other forms of chorea and can aid in the identification of the disease.

Early detection of Huntington's disease may be helped by knowledge of the family history and the expected age of onset from that in older siblings. Investigators report that the mothers of some large choreic families may be able to sense which children will develop the disease, and later events prove them to be correct.

Preliminary findings from several laboratories have sparked the hope that a test for the early detection of Huntington's disease is near, according to the National Institute of Neurological Diseases and Stroke.

#

News Feature

SALIVA HELPS SWALLOWING, DIGESTION, DENTAL HEALTH

Although taken for granted or ignored by most people, saliva gives us valuable silent services. Perhaps its most vital role is to moisten foods for swallowing. Another function is to begin the digestion of starch. Saliva also helps protect teeth from decay-causing bacterial acids, and washes away unattached bacteria that can cause disease.

This rich fluid comes from hundreds of salivary glands. The most familiar are the big parotids which swell miserably with mumps. The smaller submaxillary glands lie below the lower jaw, and the slightly smaller sublingual glands empty under the tongue. Minor salivary glands distributed around the mouth also secrete saliva.

Secretions from the various glands differ, and whole saliva is not the same as that which leaves the ducts of any one of the larger gland pairs. In addition, saliva varies between individuals, and from occasion to occasion in one individual. Also, the rate of secretion decreases sharply in the dark and during sleep. It may also change with certain emotions, drugs, and diseases.

Salivary proteins are believed to be the principal constituents of the pellicle, a microscopically thin film that forms on tooth crowns. Many bacteria cling to the pellicle with the help of other salivary and bacterial products. There the organisms form an adherent mat of plaque around the gum line. Plaque organisms are thought to be the chief causes of tooth decay and various gum diseases.

(more)

However, at the same time that saliva indirectly promotes bacterial build-up on teeth, other salivary components prevent some harmful bacteria from making themselves at home on teeth. One of these substances is a type of antibody that does not kill bacteria but makes them clump together so that they wash away.

Scientists at and supported by the National Institute of Dental Research are investigating saliva's role in health protection and disease. They are also studying saliva's effect on taste. By removing some or all of the main salivary glands in rats, they can show how secretions from each type of gland affect the animals' ability to discriminate among various concentrations of sweet, sour, salty, or bitter solutions.

Rats, like humans, prefer sweets and low concentrations of salt. They shun all but dilute acid and bitter solutions. Also, it is known that rats with very little saliva, like similarly afflicted people, can hardly distinguish among low concentrations of these four taste factors. The investigators were surprised to find that rats without parotid glands could distinguish many levels of the principal taste elements almost as well as intact rats.

However, when the other big glands were removed, the animals accepted far stronger salty and bitter solutions than before, and preferred only strong sugar solutions. They did not accept acids as predictably as animals without any of these glands. In time, animals without the main glands avoided strong bitter and acid solutions that they had previously consumed, but they never learned to control their salt intake. Perhaps they learned eventually which foods disagreed with them.

(more)

Saliva (Cont'd)

Because animals without saliva grew more slowly than intact rats even when they ate the same amount of food, scientists think that salivary glands aid digestion.

#

CANCER SPEECH--Efraim Racker, M.D., Einstein Professor at Cornell University, will deliver a National Institutes of Health Lecture on March 26 at 8:15 p.m. in the Masur Auditorium of the NIH Clinical Center. Members of the scientific community and the press are invited to attend.

Dr. Racker was awarded the NIH Lectureship in recognition of his contributions to cancer research. His address, "Ion Transport in Reconstituted Systems and in Cancer Cells," will deal with the role of proton translocation in oxidative phosphorylation. Proton translocation is believed to be the driving force in the production of biologically useful energy.

Oxidative phosphorylation is one of the most important studies in biochemistry. Dr. Racker has been involved in every aspect of the work that has been carried out on this vital process. His recent findings offer promising leads to understanding and controlling the metabolism of cancer cells.

The National Institutes of Health Lectures were established in 1953 to recognize outstanding scientific accomplishment and to contribute to the interchange of scientific information.

#

Photo Feature

Menkes' Syndrome...

BOY WITH GENETIC DISORDER BEING TREATED WITH COPPER

Twenty-month-old Jimmy is responding so well to copper treatments for Menkes' Kinky Hair Syndrome, a usually fatal genetic disorder, that he recently went home for the first time in his life.

His doctors at the General Clinical Research Center of St. Christopher's Hospital for Children, Philadelphia, believe that early diagnosis and treatment are responsible for the baby's improved developmental abilities. The research center is supported by the NIH Division of Research Resources.

Menkes' Kinky Hair Syndrome, a rare inherited trait affecting only boys, is characterized by unusual hair, severe mental retardation, deterioration of muscular control, and failure to gain weight. Other symptoms include seizures, low or absent copper levels in blood plasma, and increased susceptibility to infection. Progressive brain deterioration often reduces the child to a "vegetative" state prior to his death within the first three years of life. The kinky appearance of the victim's white, coarse hair is caused by twisted hair shafts that vary in diameter, and are broken at regular intervals. Named for John H. Menkes who described this affliction in 1962, the syndrome is associated with a defect in the passage of copper from the stomach and intestinal tract into the blood. The consequent copper deficiency seems to cause the disorder's characteristics.

Copper is an essential element in the function of many enzymes, the complex organic substances that activate specific chemical transformations in the body. Copper-dependent enzymes affect energy production, brain activity, and

(more)

physical growth, in addition to other body processes.

Scientists now believe that deterioration of the body processes from Menkes' Syndrome may begin before birth because some infants die within the first weeks of life. Previous attempts at treating children as young as three months old have been unsuccessful, possibly because of the late stage of the disease when treatment began. Jimmy began to receive copper at the age of 28 days.

Doctors hope that his response to early treatment will lead to earlier diagnosis and more effective treatment for other victims of Menkes' Kinky Hair Syndrome.

In the meantime, physicians at the NIH-supported clinical research center have changed Jimmy's outpatient treatment from intravenous to oral doses of copper with a chelating agent that helps the copper pass through the stomach and intestinal tract into the blood. It is hoped that this change will allow further improvements in the boy's development.

#

Jimmy is home for the first time in his life. (NIH Photo #1360)

New Publication:
Menopause

The National Institute of Child Health and Human Development (NICHD) brought together a group of experts in 1971 to assess what was known and accepted about the menopause, to clarify the issues regarding the use of estrogens to treat menopausal symptoms, and to determine where the gaps in knowledge of the menopause exist.

Based on that conference, NICHD has prepared a pamphlet, *Menopause*, describing the areas of concern to medical and research experts, and presenting their collective opinion on the use of estrogen therapy for treatment of this condition of aging.

Responsibility for this research will soon be passed to the National Institute on Aging. This new institute will carry forward research on the menopause as part of its mandate to conduct and support biomedical, social, and behavioral research related to the aging process and to the diseases and other special problems of the aged.

Until the National Institute on Aging is in full operation, science writers can obtain a free copy of this new publication from: NICHD, National Institutes of Health, Landow Bldg., Room A804, Bethesda, MD 20014.

#

News Releases Issued

SICKLE CELL--The National Sickle Cell Disease Program has forwarded to the Congress its Annual Report describing the current status of Program components and activities, and outlining eight goals and needs of the Program during the next five years. Among them are the needs to expand efforts to develop quicker, cheaper, and more accurate methods for detecting abnormal hemoglobins, as well as to expand investigations into the mechanisms responsible for changing production of hemoglobin from fetal to adult.

The Program, established under the National Sickle Cell Disease Control Act of 1972 (P.L. 92-294), conducts and supports research on sickle cell anemia, and carries out demonstration and education projects concerned with diagnosis, control, and treatment of this disorder, which afflicts an estimated 50,000 Americans, most of them blacks.

The 1975 Annual Report was submitted in accordance with a provision of the National Sickle Cell Disease Control Act, which requires that the National Program report each year to Congress on the administration of the Act.

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Research Advances

To Study Carotid Artery...

NEW DIAGNOSTIC TECHNIQUE IS SAFE AND NON-INVASIVE

A new, safer, and less costly technique for diagnosing a common problem often leading to strokes has been reported by a team of Massachusetts Institute of Technology (MIT) and Massachusetts General Hospital (MGH) investigators.

The first trial of "phonoangiography" has yielded encouraging results. A member of the team told the annual meeting of the American College of Cardiology in February that in a 48-patient study at the MGH, the technique compared favorably with the traditional method, arteriography.

All 48 patients suffered from stenosis (narrowing) of the carotid artery, the main conveyor of blood to the brain. Caused by a buildup of fatty deposits on the artery's inner wall, this condition can obstruct blood flow, often leading to a stroke. The underlying disease process, known as atherosclerosis, affects millions of Americans.

James O. Gruber, an MIT graduate student, told the gathering that when the artery had shrunk to half its normal size or less, phonoangiography proved capable of measuring the amount of narrowing. Patients with milder stenosis generally lack symptoms and do not seek medical attention.

The senior investigators, Robert S. Lees, M.D., and C. Forbes Dewey, Jr., Ph.D., began work on the technique five years ago. Phonoangiography involves recording the noise produced by blood flow in the affected artery and feeding the sound into a minicomputer for analysis.

This process offers a number of advantages over arteriography, the method now widely used to examine patients with suspected carotid artery

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stenosis. During an arteriographic examination, the physician threads a catheter (hollow tube) into the patient's artery, passes a special dye through, and takes a rapid series of X-ray pictures. This method requires hospitalization, causes some discomfort, and poses a slight risk to the patient.

Phonoangiography, however, is "noninvasive." It entails no probes into the body. Since the physician can perform the test on an outpatient basis, the procedure is likely to cost the patient far less than the conventional examination.

Although he does not expect the new technique to replace the older one, Dr. Lees anticipates that phonoangiography will become a screening procedure. "By weeding out patients who do not need arteriograms," he explained, "it could cut down on the number performed."

Phonoangiography should make it possible to examine one patient repeatedly. Previously, the discomfort associated with arteriography discouraged both physician and patient from doing this as often as it might have been to evaluate the effects of treatment and study the course of the disease.

Phonoangiography depends on the principle that a constricted blood vessel produces turbulent flow, which in turn yields sound varying in pitch and loudness with the degree of narrowing. Physicians have long suspected that this was the case. On hearing fairly high-pitched sound while examining a patient with a stethoscope, they suspect that stenosis has become advanced. Phonoangiography, however, offers a quantitative measure of the narrowing.

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Carotid Artery (Cont'd)

To perform the test, the physician simply places a pressure-sensitive microphone on the patient's skin over the artery and records the sound on tape. The computer then analyzes this sound, minimizing background noise, and exhibits the results on a cathode ray tube.

The tube display breaks the sound down into individual pitches, showing the loudness of each. Using the loudest single pitch and the speed of blood flow in the artery, the physician can estimate the diameter of the artery.

Typically, the results of a phonoangiographic examination reveal loudness increasing with pitch to a single point and then rapidly falling off. If a test does not produce such a pattern, it cannot be analyzed. The MGH-MIT investigators said, 11 of the 61 tests from 48 patients produced unusable results.

During patient trials conducted at the MGH, researchers compared artery measurements obtained through arteriography. In the first 25 studies the investigators found that the new test came within one millimeter of the arteriograms 73 percent of the time. This percentage rose to 84 in the second group of 25 studies. The unobstructed carotid artery measures roughly eight millimeters in diameter.

The greater success with the second group resulted from a modification in the system to take account of the actual velocity of the artery blood in each patient. In calculating artery diameter the investigators had at first used the normal velocity of blood in the artery. Speed of flow falls, however, in very severe stenosis.

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Carotid Artery (Cont'd)

The MGH and MIT investigators have begun work on phonoangiographic examinations for the aortic valve, through which blood flows on leaving the heart, and for the femoral artery, which feeds the legs. The scientists are also attempting to improve the carotid artery test.

For this procedure, the research team has included a number of MIT engineers, MGH cardiologists, neurologists and neurosurgeons, and a Draper Laboratory team which developed the computer system.

The development and testing of phonoangiography has derived research support in part from the National Heart and Lung Institute.

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CHIMP "DENTISTS"--Chimpanzees at the Delta Regional Primate Research Center inspect, clean, and extract their own and each other's teeth. In their practice of "dentistry," the animals make and use stick tools to supplement the use of their fingers. This represents the first example of repeated tool use by animals in social grooming, according to the National Institutes of Health.

IMMUNOTHERAPY REGISTRY--An International Tumor Immunotherapy Registry has been established by the National Cancer Institute to serve as a center for collection, storage, and exchange of information on immunological methods of treating cancer. The Registry will record physicians' experience with immunotherapy for human cancer, including methods of administration, results of the treatment, and possible side effects.

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Research Advances

SCIENTISTS USE NEW TECHNIQUES TO GROW LYMPHOMA CELLS IN LAB

New techniques have enabled two scientists to grow in the laboratory tumor cells from lymphoma patients. This is the first time human lymphoma cells have been grown successfully in culture, except for Burkitt's lymphoma (a cancer found in African children).

Lymphomas are cancers of the lymph glands. The tumor cells grown by the researchers came from three patients with histiocytic lymphomas, one of the most malignant cancers of the lymphoma group.

The establishment of cell cultures from human tumor biopsy specimens has been difficult because dividing tumor cells require a critical combination of nutrients, growth factors, and environmental conditions to grow outside the human body.

The researchers, Alan L. Epstein and Henry S. Kaplan, M.D., said their success was due to the development of new cell culture methods that enabled the rapid testing of a large number of factors. By dividing the patients' tumor cells into small samples and storing them at low temperatures, the scientists were able to test each biopsy specimen repeatedly until the growth requirements of each tumor were uncovered.

The research, funded in part by the Virus Cancer Program of the National Cancer Institute, will provide an important new source for laboratory investigation. The cell technique will lead to improved treatment and diagnostic methods of lymphomas.

The cells may also be used in a search for cancer-inducing viruses and in finding ways for stimulating natural immunity against cancer.

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Lymphoma Cells (Cont'd)

The establishment of these human malignant cells in culture is of particular importance, the scientists said, because the cells are free of the Epstein-Barr virus, which has been found to pass onto normal white cells the ability of continuous growth in the laboratory.

Establishing a lymphoma cell line uncontaminated by the Epstein-Barr virus has been a major challenge because the virus is present in many people, including lymphoma patients, for most of their lives.

The researchers said the cultured cells were strikingly similar to the patients' tumors from which they were taken. "The malignant cells had the same chromosomal abnormalities and were capable of widespread growth when inoculated into the brains of 'nude mice,'" they reported.

These hairless mice are used because they lack a thymus gland and therefore do not have cellular immunity to destroy the implanted cells. It is well accepted, the researchers explained, that when such transplanted cells "take" and proliferate, they are malignant.

Epstein is a medical and graduate student at Stanford University School of Medicine, and his work is supported by the Medical Scientist Training Program of the National Institutes of Health. Dr. Kaplan is a professor of radiology at the medical school and a pioneer in cancer research.

Epstein and Dr. Kaplan published their findings in the December 1974 issue of *Cancer*, the journal of the American Cancer Society.

Note to Subscribers

This story was prepared by Susan Johnson, a University of Maryland senior, now a U.M. intern in NIH News Branch.

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Research Advances

IDU IS INEFFECTIVE IN TREATING HERPES ENCEPHALITIS PATIENTS

Two carefully controlled studies of the efficacy of IDU (5-iodo-2'-deoxyuridine) in treating herpes encephalitis patients have revealed no benefit from the drug. The investigators, whose work is partially supported by the National Institute of Allergy and Infectious Diseases (NIAID), terminated the studies prematurely when IDU therapy failed to prevent death and when unacceptable levels of bone marrow suppression occurred.

Herpes simplex virus (HSV) encephalitis is such a lethal disease that many attempts have been made to develop a successful form of therapy. IDU is an investigational drug which has been frequently reported as being successful in altering the severity and mortality of HSV encephalitis.

However, because dosages and schedules of administration have varied and cases treated have not always been definitively diagnosed, it has been difficult to assess, reliably, the efficacy of IDU. Consequently, in late 1971 and early 1972, two placebo-controlled, double-blind multi-center studies were independently initiated. One was carried out by a group of physicians in Boston area hospitals; the other, by investigators representing some 18 institutions enrolled in a NIAID-sponsored Cooperative Antiviral Clinical Study. The latter group, led by C.A. Alford, M.D., of the University of Alabama is also engaged in evaluating another antiviral, adenine arabinoside, under contract to the Institute.

Twelve critically-ill patients who, on clinical grounds, were thought to have HSV encephalitis underwent brain biopsy to establish the diagnosis, and were enrolled in the two studies. Six of these patients were proven to have

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the disease, three were considered probable cases, and three were considered doubtful. The nine patients with proven or probable HSV encephalitis were given IDU (or placebo) intravenously at a dose of 100 milligrams per kilogram of patient body weight for five days. The three doubtful received the drug for only three days.

Seven of the nine patients died following completion of therapy. One survived with severe neurological deficit, while the other patient recovered and is apparently normal except for recurrent seizures. The three doubtful cases survived but two have neurologic complications.

Despite a full course of the drug, virus could still be isolated from the brain in all four biopsy-proved cases in which post-mortems were done. In two patients, it could be shown that the quantity of virus present was equal to or greater than that present before initiation of IDU therapy.

Significant toxicity was not observed in any of the three doubtful HSV patients nor in the one probable HSV encephalitis patient who received placebo. The bone marrow was seriously depressed, however, in six of the eight patients who received a full course of therapy. Such depression can be life-threatening in itself since it renders patients extremely vulnerable to serious infections.

Although the investigators speculate that IDU treatment initiated early in the course of HSV encephalitis might be more successful than the regimen used in this study, they conclude that, until appropriate data emerge, IDU should not be used to treat HSV encephalitis.

A joint report on these studies was published in the March 20, 1975, issue of the *New England Journal of Medicine*.

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Research Advances

SCIENTISTS STUDY GALLSTONES FOUND IN SQUIRREL MONKEYS

Scientists at the Oregon Regional Primate Research Center, one of seven primate centers supported by the Division of Research Resources, are studying gallstone formation in atherosclerotic squirrel monkeys to better understand the relationship, if any, between the two diseases. The squirrel monkey is susceptible to both conditions and is therefore an excellent research model for scientists to gain insight into the causes and possible connection of these problems in man.

The researchers look at the therapeutic approaches to the two diseases which sometimes exert different and reverse effects. For example, the use of unsaturated fats and drugs to lower the blood cholesterol level as a protection against atherosclerosis increases the possible risk of gallstones. On the other hand, certain chemical agents used to prevent gallstone formation such as chenodeoxycholic acid can affect the course of atherosclerosis.

To identify the factors that affect gallstone formation, the scientists varied the type and level of fat, included or removed cholesterol, varied the source of carbohydrate, and added cellulose to the diet. They found that in most cases, those diets that contained cholesterol resulted in the formation of gallstones in the monkeys. But at this point, the researchers are still investigating the importance of dietary cholesterol in human gallstones.

There are many similarities and differences between cholesterol gallstone disease in humans and squirrel monkeys in such aspects as stone structure, bile composition and physiology, and response to diet. But these only increase the importance of the Primate Center's animals as research models

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for the many diseases that plague man.

The researchers--O.W. Portman, M.D., T. Osuga, M.D., N. Tanaka, M.D., and M. Alexander--published a report of their studies in the January issue of *Primate News*.

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DENTAL IMPLANTS--Implants are non-living materials placed in the body to substitute for damaged or missing parts. For the past 20 years, some researchers have investigated surgical metals, plastic covered metals, acrylic plastics, and ceramics as dental implants. However, the National Institutes of Health does not recommend any type of tooth implant for public use.

DENTAL REPLANTS--Replants are teeth that have been knocked out by accident and then are replaced in the same socket. According to the National Institutes of Health, the replant procedure is relatively simple, often painless, and works most effectively on a child's tooth which has been out of the mouth less than an hour.

DENTAL TRANSPLANTS--Dental transplants are natural tissues or organs which are inserted as a replacement for a missing tissue or organ, coming from the same person or from someone else. National Institutes of Health studies have shown that soaking the tooth in a fluoride solution may prolong the success of the transplanted tooth. The researchers are now studying methods of transplanting teeth between siblings with closely matched tissues in an effort to slow rejection and prolong tooth survival.

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Research Advances

CAUSE OF INFANT BACTERIAL MENINGITIS IS IDENTIFIED

Houston scientists have identified type III strains of group B streptococci as the major cause of infant bacterial meningitis and of blood poisoning in infants over 10 days old. This finding supports the theory that certain types of strep are associated with distinct diseases and further suggests that type III may have special properties which allow it to invade the meninges, the membranes that envelop the brain and spinal cord.

In the past few years, group B strep has been recognized as a major threat to the newborn, producing two distinct clinical illnesses in infants depending upon their age at onset of infection. The early type occurs in newborns five days of age or younger and is acquired from the mother during birth. This highly fatal form of blood poisoning--with or without meningitis--is also characterized by respiratory problems, particularly pneumonia. The mortality rate is lower in infants 10 days of age or older who acquire late onset blood poisoning--with or without meningitis. The source of this infection is still unknown.

To determine whether these variations in infant group B strep infections are caused by different types of the organism, scientists at Baylor College of Medicine, in work supported by the National Institute of Allergy and Infectious Diseases, studied 169 infants hospitalized over a 42-month period. One group of 53 infants had no evidence of infection although group B strep was isolated from samples obtained by swabbing their throats, umbilical cords, or ears. All group B serotypes were detected in these samples, with types II, III, and Ia the most frequent. However, the incidence of particular types has been

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shown by other studies to vary according to time and geographic location.

In 62 infants with early onset blood poisoning, types II and III were the most prominent (44 percent and 33 percent respectively). However, only type III was isolated from six infants with late onset blood poisoning, and type III strains were also the major organisms in 48 infants with either early or late onset meningitis (80 percent and 93 percent respectively).

The investigators, Carol J. Baker, M.D., and Fred F. Barrett, M.D.,--believe that this striking predominance of type III strains in late onset blood poisoning and in meningitis suggests a difference in the epidemiology of late and early onset infection. Furthermore, except for the prevalence of type III, infants with early onset meningitis are clinically indistinguishable from those with early onset blood poisoning. This finding indicates that the spread of infection from the blood to the meninges may be due to an inadequate immune response to the type III strains by the patient.

The researchers believe that future studies should concentrate on the acquisition of late onset infections as well as the disease mechanisms of early and late meningitis. In addition, the precise relationship between antigenic components of type III strains may provide insights into the difference in these infant diseases.

These findings were reported in the November 25, 1974 issue of *The Journal of the American Medical Association.*

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Research Advances

Background Report...

NEW VACCINES AGAINST HEPATITIS B FOUND SAFE, EFFECTIVE IN CHIMPS

NIH scientists have developed a method for producing vaccines against hepatitis B which were safe and effective in tests in chimpanzees.

The investigators, Robert Purcell, M.D., and John Gerin, Ph.D., believe their work provides a strong, scientific base for expanded studies of hepatitis B immunization, now underway at NIH and in other laboratories. Vaccines against hepatitis B, or serum hepatitis, are needed particularly for use in high-risk groups such as members of the Armed Forces, patients and personnel of hemodialysis units, and residents of institutions.

Starting material for the model vaccines is serum or plasma from a human chronic carrier of the hepatitis B surface antigen, formerly known as the Australia antigen. This antigen, occurring in several subtypes, is shared by the Dane particle--now believed to be the actual virus of hepatitis B--and by much smaller spherical particles found in abundance in the blood of hepatitis B carriers.

Dr. Purcell, of the Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases (NIAID), and Dr. Gerin, of the NIAID-AEC Molecular Anatomy Program Laboratory, used a three-step procedure to remove or inactivate infectious hepatitis B virus (HBV) in the starting human material. First, all Dane particles were removed by centrifugation. The remaining, small, non-infectious particles were then purified by centrifugation. As a final precaution, the purified particles were inactivated by treatment with formalin--a chemical successfully used in the preparation of a number of

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inactivated virus vaccines.

The potency of the prototype subunit vaccines was tested in guinea pigs and it could be shown that hepatitis B surface antigen had been recovered from the human serum and that the vaccine, though inactivated, was still capable of inducing the formation of specific antibody.

Safety tests were carried out in seronegative (unexposed) chimpanzees. Six animals were infants born and raised at Holloman Air Force Base in New Mexico in a cooperative program jointly sponsored by NIAID, the Bureau of Biologics, FDA, and the Center for Disease Control. One chimpanzee was a jungle-caught animal housed at the Delta Primate Center in Louisiana, under an NIAID contract.

John L. Gerin, Ph.D., director of the NIAID-AEC Molecular Anatomy Laboratory, Rockville, MD, inserts a rotor into a zonal centrifuge, located inside the Glove Box. Such a centrifuge is used to separate and remove the infectious Dane particles from the smaller non-infectious particles in the blood of hepatitis B carriers. These smaller particles have been used in an experimental hepatitis B vaccine recently shown effective in protecting chimpanzees from this disease. (NIH Photo #1361)

Six chimpanzees were given one of the following: a formalin-inactivated vaccine for the ayw subtype; the same vaccine, not exposed to formalin; the hepatitis B antigen positive serum from which the ayw vaccine was made; a formalin-inactivated adr vaccine; or the solution used as the diluent for the vaccines. One animal was given no material and was later used as a control in efficacy tests.

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The vaccines were given subcutaneously in two doses, one month apart. The ayw-containing serum was administered intravenously. Serum samples were obtained weekly from all the animals and tested for hepatitis B surface antigen and antibody and for antibody to the hepatitis core antigen (which is found only on the Dane particle).

None of the vaccinated animals showed any signs of hepatitis B infection, but did develop antibody to the hepatitis B surface antigen. The one chimpanzee given the untreated ayw serum actually developed hepatitis B.

Efficacy tests of the vaccines were carried out six months later in both vaccinated and control animals, all of whom were given infectious doses of hepatitis B virus, subtype ayw intravenously.

The two unvaccinated chimps developed hepatitis B. None of the ayw vaccinees had any biochemical or serologic evidence of HBV infection. The adr vaccinee became infected but did not develop signs of disease, indicating possibly, that the severity of his disease had been blunted by administration of the adr vaccine.

In presenting results of their work, Drs. Purcell and Gerin pointed out that preparation of a vaccine from antigens not grown in tissue culture is novel but not without precedent, as in Jenner's vaccine for smallpox and Pasteur's for rabies.

Although there has been no evidence, to date, of any harmful effects of the vaccines, additional studies are needed and are being conducted.

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Photo Feature

CORNEAS STORED IN NEW MEDIA USEFUL AT LEAST SEVEN DAYS

University of Florida ophthalmology researchers have developed a simple, inexpensive technique for refrigerator storage of corneal tissue.

Donated corneas may be kept fresh and viable in the nutritive liquid for at least seven days. Previously, eyes donated for transplantation had to be used within 24 to 48 hours following removal or stored under cryopreservation, a freezing technique, requiring expensive equipment and specially trained technicians.

With the new technique, even small eye banks with limited funds will be able to store donor eyes in the liquid and schedule corneal transplant surgery under optimal operating conditions at the convenience of both patient and surgical team.

The new solution, named M-K Media after its developers, Bernard E. McCarey, M.D., assistant professor of ophthalmology, and Herbert E. Kaufman, M.D., professor and chairman of the department of ophthalmology, is being made available to eye banks throughout the nation free of charge.

Before the media was used for human cornea transplants, rabbits served as the primary animal model for receiving transplanted corneas which had been preserved in the media. Clinical data indicates that corneal tissue stored in the M-K Media holds up as well as tissues stored under cryopreservation or freshly removed from the donors.

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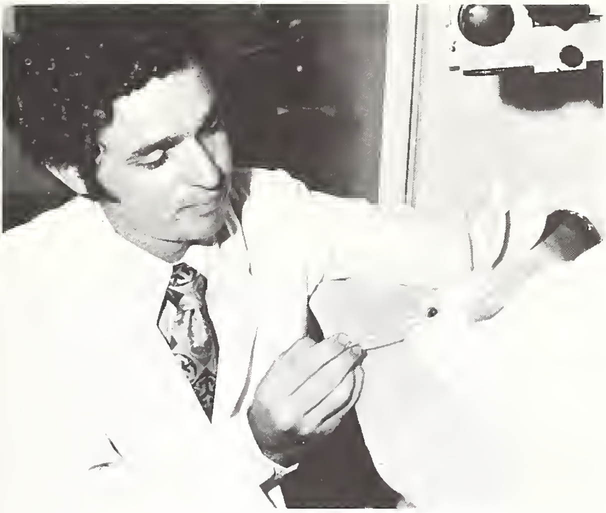
Corneas (Cont'd)



Dr. Bernard McCarey, assistant professor of ophthalmology at the University of Florida, assesses rate of healing in a rabbit which received corneal tissue preserved in the nutritive solution he developed. Corneal tissue stored in the special liquid remained fresh and viable and resulted in successful transplantation in animal models. (NIH Photo #1362)

The new preservation technique has been adopted recently by the Medical Eye Bank of Maryland in Baltimore which serves Johns Hopkins University, the Eye Bank for Sight Restoration which serves several hospitals in New York City, and several other large city eye banks. Perry Binder, M.D., a former clinical fellow in ophthalmology at the University of Florida, is introducing the new technique to physicians in Bangladesh, through an exchange program sponsored by the International Eye Bank in Washington, D. C.

The cryopreservation technique, introduced by Dr. Kaufman in 1965 as the first successful technique for long-term storage of corneal tissue, will continue to be used by large medical centers where many corneal transplants are performed and where donor eyes are stored for months or years for emergency surgery and eye research.

The M-K Media is described by its developers as a nutritionally complete solution comprised of amino acids, glucose, salts and other nutrients, along with dextran which prevents corneal tissue from

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Corneas (Cont'd)

absorbing water. A newly donated eye is simply rinsed in an antibiotic solution, after which the cornea is removed and dropped into the bottled media solution and stored at four degrees centigrade. When taken out of refrigeration, the cornea may be lifted from the media with sterile forceps and used immediately for transplantation.

This research is supported by the National Eye Institute.

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Success in animal research led to eventual storage of donor eye tissue for use in human corneal transplantation. A cornea which had been kept viable in the McCarey-Kaufman Media (above) is lifted from sterile bottle with sterile forceps and transferred to surgeon who will perform delicate transplant procedure. (NIH Photo #1363)

Photo Feature

NHLI DEDICATES SICKLE CELL EXHIBIT AT CHICAGO MUSEUM

Theodore Cooper, M.D., Acting Assistant Secretary for Health, DHEW, cut the ceremonial ribbon to officially open the new sickle cell exhibit on the medical balcony of the Museum of Science and Industry in Chicago on March 24.

The 1,000-square-foot educational display is the first and only permanent sickle cell exhibit in the world. It was developed by the Comprehensive Sickle Cell Center at the University of Chicago in collaboration with the Museum. Funds came from the Sickle Cell Disease Branch of the National Heart and Lung Institute.

The four-panel display leads the viewer past a lighted map showing the geographic origins for sickle cell; by a series of revolving lighted wheels

Press people who attended the ribbon-cutting ceremony (left photo) performed by Dr. Cooper asked him several questions (right photo) about the sickle cell exhibit and about the 15 Comprehensive Sickle Cell Centers that are funded by the National Heart and Lung Institute. (NIH Photos #1364, 1365)

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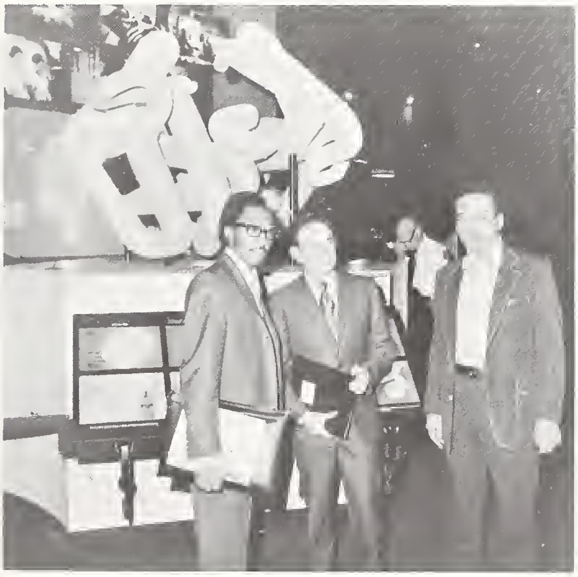
Dedication (Cont'd)

that depict the genetic chances for having the disease; around a lighted rotating six-foot multi-dimensional model of a hemoglobin molecule, past lighted panels showing the physical manifestations of sickle cell disease, and to a six-minute color motion picture that explains how the disease affects the body.

In his remarks at the opening, Dr. Cooper praised the exhibit as a definitive educational effort to dispel the many misgivings surrounding the sickle cell problem. He said, "We will continue our commitment to support the National Sickle Cell Disease Program."

The exhibit will be maintained by the Museum of Science and Industry for at least five years and then continue as long as there is public interest.



Dr. Cooper toured the sickle cell exhibit (left photo) with Rudolph Jackson, M.D., (left), program coordinator of the National Sickle Cell Disease Program, and James E. Bowman, M.D., (right), director of the University of Chicago Comprehensive Sickle Cell Center. (The same men appear on the cover photo.) Through displays, recordings, and a film, the exhibit is designed to educate adults, students, and youngsters about sickle cell research. The exhibit will remain at the Museum of Science and Industry for at least five years. (NIH Photos #1366, 1367)

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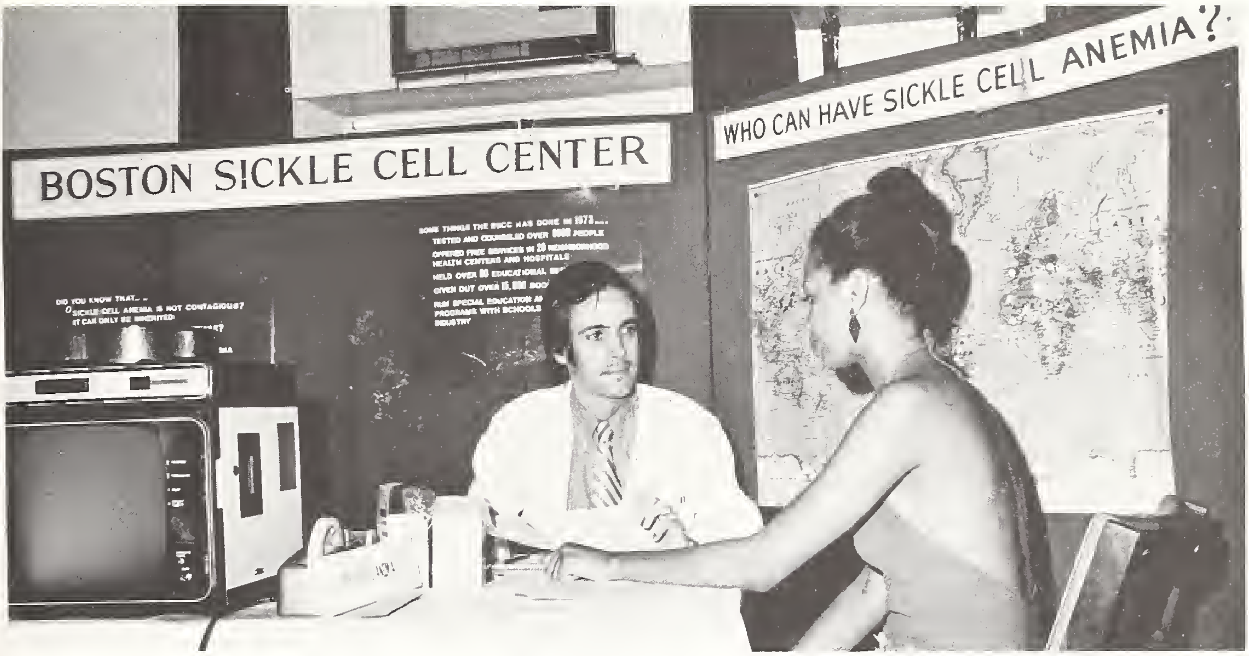
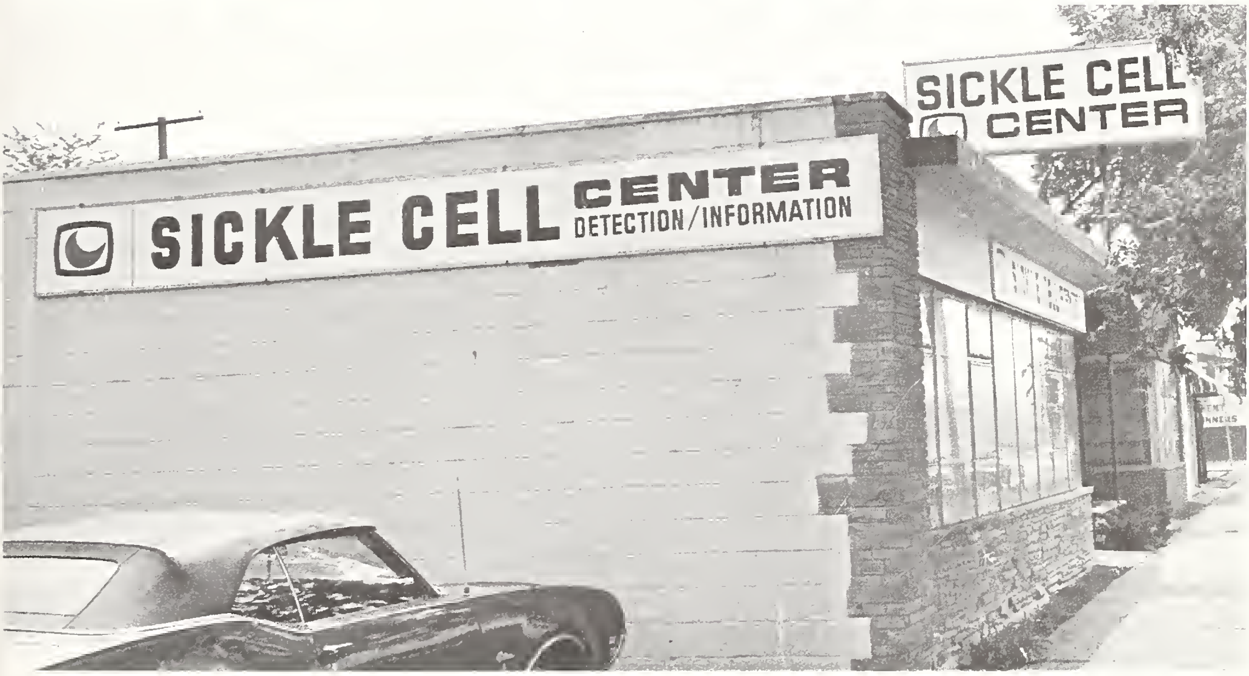
Dedication (Cont'd)


BOSTON SICKLE CELL CENTER
WHO CAN HAVE SICKLE CELL ANEMIA?



The 15 Comprehensive Sickle Cell Centers supported by the National Heart and Lung Institute are involved in research projects and education programs. Two of the cities with Centers are Boston (top photo) and Detroit (bottom photo). (NIH Photos #1368, 1369)

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News Feature

Evidence Builds...

EPSTEIN-BARR VIRUS MAY BE MONO CAUSE

The National Institute of Allergy and Infectious Diseases (NIAID) is supporting research into the causative agent of infectious mononucleosis (mono). Many of these studies are focused on a "herpes-like" virus known as the Epstein-Barr (EB) virus. Evidence is building that the EB virus is the cause of mono.

In NIAID-supported studies, scientists have made the following important observations after studying blood samples drawn from university students: young people whose blood lacked antibodies to the EB virus are susceptible to mono while those whose blood contained EB virus antibodies when they entered college are not; EB virus antibodies regularly developed in the blood of students who experienced mononucleosis; and for every two cases of mono diagnosed in college, there is one case of inapparent infection.

Other studies have shown EB virus to be present in cultured lymphocytes obtained from mono patients' blood. Using immunofluorescence and electron microscopy techniques, investigators have identified the virus and shown that it can be found there for years after infection.

In another study partially supported by NIAID, scientists at Yale University found that throat washings from mono patients inoculated into a culture of human leukocytes transformed those cells into ones with unlimited growth potential in culture. EB virus, used in the same way, produces a similar result, but throat washings from people without mono do not.

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Two lines of evidence indicate strongly that the transforming agent present in the throat washings of mono patients is EB virus and that this is the cause of infectious mononucleosis. First, the investigators detected virus-specific antigens (substances that induce the formation of antibodies) in the leukocytes transformed by the throat washings and by EB virus. Secondly, they found that the transforming activity of the throat washings was destroyed by antibody to EB virus.

An unexpected finding of this study was that the transforming agent (presumably EB virus) was found in the throat washings for prolonged periods after the patients had acute infectious mononucleosis. It was present regularly two to five months after clinical illness. In one case it was detected 16 months after the disease had occurred.

The presence of this persistent carrier state of EB virus may explain why it has been so difficult to trace transmission of infectious mono on a case by case basis. In one study only 14 percent of mono patients gave a history of contact with other mono patients. These findings also lend further support to the hypothesis that the disease is spread by the oral route, through intimate contact, such as kissing.

No other virus has been found to be associated with mono in these ways, and EB virus has not been connected to any other infectious disease. Drs. Epstein and Barr, two British scientists for whom the virus is named, first found evidence of EB virus in patients suffering a rare form of cancer--Burkitt's lymphoma--which occurs mainly in children in the warm, rainy lowlands of Africa. Recently, antibodies to the virus have also been found

(more)

in patients with nasopharyngeal cancer. Because the role of this virus in the development of cancer is unknown, investigators do not want to use it for studies of mono transmission in humans. In research in animals, however, EB virus has not reproduced any mono-like infection.

In addition to the possible viral connection between mono and certain cancers, other features of mono are suggestive of malignancies such as leukemia and lymphoma. Studies of the body's response to mono may provide a link between normal lymphocyte reactions and cancerous ones.

For some time there was speculation that infectious mononucleosis might be an abortive form of acute lymphatic leukemia; but recent reports of children who have developed both diseases concurrently suggest that infectious mono is etiologically unrelated to acute leukemia and that it may even have some beneficial effects on the leukemia patient. Scientists have hopes, however, that information gained from studies of mononucleosis will shed light on the problems of leukemia as well.

Scientists now suspect that clinical symptoms of mononucleosis may be the result of an over-exuberant immune response in someone susceptible to EB virus infection. Thus, one approach researchers are now taking to mono is to explore how this infection affects the two arms of the body's protective system--cell-mediated immunity (associated with T-cells) and humoral immunity (based on B-cells).

The results of a preliminary study in this area supported in part by an NIAID training grant were recently reported by investigators at the University of New Mexico. Using blood samples from a small group of mono patients, these

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scientists showed that the number of T- and B-cells in the blood increased significantly during the illness, especially during the first three or four weeks, and then decreased again as the patients recovered. However, there was no change in the proportion of these two types of cells in the blood.

These investigators were not able to determine whether the atypical lymphocytes--the hallmark of mono--originate from T- or B-cells or how these two systems interact during a mono infection. Some researchers believe that a faulty interaction between the two types of immunity occurs during mono and that cell-mediated immunity is somehow depressed during the early stages of the disease. Other investigators suggest that the atypical cell is a "T-cell," but that the virus is present in "B-cells." Further investigations are progressing in attempts to answer these questions.

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SPREAD OF TOXOPLASMOSIS--Cockroaches and wild cats may join the domestic cat and other animals as carriers of toxoplasmosis, a widespread parasitic infection found throughout the world. Scientists at the National Institute of Allergy and Infectious Diseases and investigators supported by the Institute report new evidence implicating these species in the transmission of the toxo organism. Although usually a mild disease, toxoplasmosis can be extremely serious in pregnant women who contract it. Like German measles, toxoplasmosis may cause congenital defects in an unborn child, while causing a mild or symptomless disease in the mother. More than one-third of all adult Americans are infected by the toxo organism at some time during their lives.

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Photo Feature

UTAH INVESTIGATORS DEVELOP WEARABLE ARTIFICIAL KIDNEY

Scientists at the University of Utah have developed a wearable artificial kidney which should be available for general use within two years.

The seven-pound device will be a welcome and needed addition to the various types of artificial kidneys currently available for use by persons who have lost the function of their kidneys through disease or injury.

According to the researchers, the new artificial kidney will make dialysis cheaper and less damaging to a patient's blood; it will also give freedom of movement to users who presently have to remain connected to a larger, stationary artificial kidney machine during conventional treatment. The wearable artificial kidney can be produced for considerably less money than conventional dialysis units. It was developed with the support of the Artificial Kidney Program of the National Institute of Arthritis, Metabolism, and Digestive Diseases.

Robert Stephen, M.D., of the home dialysis training center at the University of Utah hospital indicates that a patient using the portable unit would undergo dialysis every day instead of three times weekly, thereby maintaining a more even chemical balance in his blood and tissues and preventing a buildup of waste products.

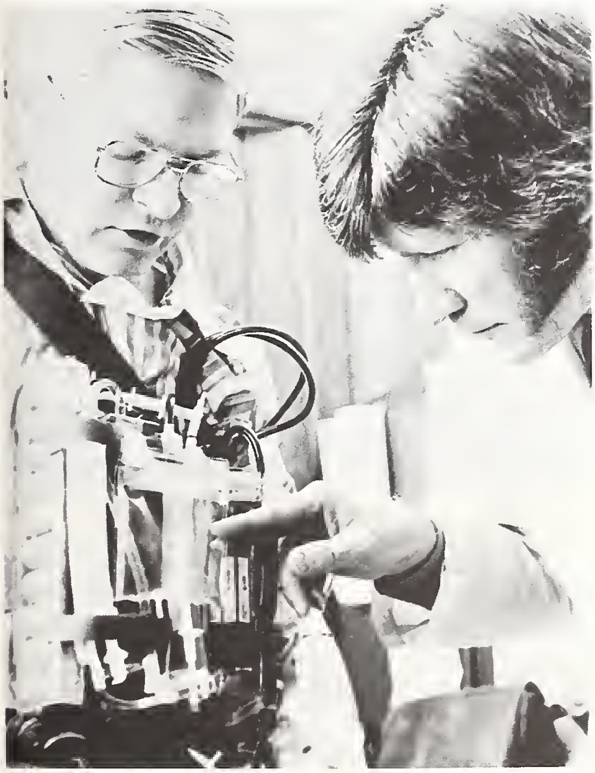
In its present development stage, the portable artificial kidney cannot remove urea, a major waste product, from the blood, according

(more)

to Dr. Stephen. Therefore, in addition to using his portable unit two hours a day while moving about freely, the patient will spend one hour with the unit hooked to a stationary 20-liter tank to remove urea.

A Salt Lake City firm will soon begin producing the novel small pump for the portable, battery-powered unit so that it can be used with conventional home dialysis machines. The investigators expect to see production of the dialyser and spare components within a year.

The wearable artificial kidney has been in the design stage for two years, and it will take at least another two years before all the portable unit components will be manufactured for purchase.



Technician Edwin Bulloch (right) examines a wearable artificial kidney worn by a dialysis patient. (NIH Photo #1370)

#

Photo Feature

COMPUTERS MONITOR PATIENT CONDITION

An NIH computer systems analyst is shown viewing the display of a patient's electrocardiogram (ECG) on a cathode ray tube. The ECG is collected at the patient's bedside using a specialized electronic cart. The electric signals are then converted into a form which can be processed by the computer. After the ECG has been entered into the machine, a computer program analyzes the characteristics of the ECG and prints out a report for the physician, identifying any abnormality which has been discovered. However, there is always a chance of equipment malfunction or electronic interference with the ECG signal. Consequently, the systems analyst periodically checks the ECG display in order to correct and identify problems as they occur. The entire process requires close collaboration between physician, patient, and computer expert and is part of a research project conducted at the NIH Division of Computer Research and Technology. Many large medical centers across the country are implementing similar computer systems to analyze patient data. (NIH Photo #1371)

#

New Publication:
Pharmacology Research Associate Program of the National Institutes of Health

The Pharmacology Research Associate Program of the National Institute of General Medical Sciences offers postdoctoral research experience to promising investigators in the clinical or basic sciences.

Application deadline is April 18, 1975, for the two-year appointments beginning July 1, 1976. Interviews will be conducted by invitation at NIH June 16 through 27. Selection will be made in July.

For more information on this program, copies of the new NIH publication, *Pharmacology Research Associate Program of the National Institutes of Health*, can be obtained from:

Dr. Byron B. Clark, Director
Pharmacology Research Associate Program
National Institute of General Medical Sciences
NIH-Westwood Building, Room 9A-05
Bethesda, MD 20014
Phone: (301) 496-7707

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Research Advances

In Congenital Pseudarthrosis...

NEW TECHNIQUE HELPS BONE REGENERATION IN CHILDREN

A Columbia University scientist has described a new therapeutic technique that has successfully promoted bone regeneration in children with congenital pseudarthrosis ("false joint").

Developed during research supported by the National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD), the new technique uses low-frequency, low-intensity electromagnetic fields coupled to tissue by application to overlying skin.

In recent years several different NIAMDD grantee scientists have described some success with bone fracture healing in response to electrical stimulation by electrodes implanted within the bone near the fracture site. Such patients suffered from either a long-term non-healing fracture, or from a congenital pseudarthrosis that was refractory to pinning, grafting, or fusion.

Now, the Columbia researcher, C. Andrew Bassett, M.D., has successfully promoted bone regeneration in five children with congenital pseudarthrosis, utilizing an electromagnetic technique that requires no electrode implantation or large voltage. Good union of the fracture, with no recurrence of the disease, was observed in all five patients, with the first patient having been followed for as long as 18 months.

Each child had previously undergone multiple, unsuccessful operations for his or her intractable type of nonunion of the tibia and was facing amputation. Following in-hospital casting, a pair of coils was placed in

(more)

windows in the cast on either side of the fracture. When pulsed with 24 to 30 volts, the coils supply a magnetic field at right angles to the bone, which induces a voltage near the fracture site.

The first patient was treated for 16 hours a day at home for four months. Bone healing was confirmed both clinically and by X-ray; remodeling of bone, bridging of the defect, and return of function were monitored. The patient's congenital pseudarthrosis has since remained stable for 18 months and she has been ambulatory. The other children have had no disease recurrence after four to seven months.

Although the mechanism of electromagnetic action is still unclear, healing is believed to involve a complexing of cations (positively charged ions) such as calcium and potassium, and their release from binding sites following electromagnetic radiation. The investigator suggests that his technique might ultimately be applicable to routine fractures and may cut healing time by as much as 50 percent.

Dr. Bassett of the Columbia University College of Physicians and Surgeons reported his findings in the *Annals of the New York Academy of Sciences*, January 1975.

#

MONKEY CENSUS--The National Institutes of Health conducted a survey of worldwide primate populations to determine the future availability of primates for medical laboratory studies. A shortage of monkeys and apes for research is expected within the next five to 10 years. This could necessitate the breeding of all subhuman primates by investigators.

#

Research Advances

Muscular Dystrophy Studies...

MUSCLES OF ROUND WORMS MAY YIELD RESEARCH CLUES

The muscle structure of a common round worm may give researchers clues to understanding muscular dystrophies that cause gradual paralysis in humans, according to a California scientist.

Studies in the nematode, a round worm, have shown for the first time that molecular defects in the structure of the muscle tissue can lead to defects in the function of that muscle.

The research is being done by Henry Epstein, M.D., at Stanford University School of Medicine, and by Sydney Brenner, M.D., and Robert Waterston, M.D., and J.N. Thomson, all of the Medical Research Council Laboratory in Cambridge, England. Their work is reported in the recent *Journal of Molecular Biology*, and in *Nature*, a British scientific journal, January 23, 1975.

Normal muscle viewed end on end, consists of a lattice of thick protein filaments surrounded by thin protein filaments, all in a very definite unvarying pattern. But the muscle of certain mutant nematodes who have been paralyzed by early exposure to high temperatures is conspicuously different, with thin filaments set at all angles, randomly, instead of being in parallel.

Scientists are investigating whether the fault lies perhaps in some protein which acts during the assembly of the muscle components--whether some slight alteration in the chemical composition of the enzyme prohibits it from performing its function as an enzyme.

Another set of mutant nematodes studied have severe paralysis at all temperatures and throughout their lifespan.

(more)

Round Worms (Cont'd)

"We traced the genetically-defective muscle back to disruptions in the filament lattice-work responsible for contraction, and to the myosin molecule, which is the "engine" for contraction," says Dr. Epstein.

Errors in the myosin molecule can prevent formation of normal thick protein filaments which in turn prevent development of normal structure and function within the muscle, according to Dr. Epstein.

Scientists who have been working on dystrophic muscle for many years have not been in agreement whether defects are in the nervous system or in the muscles. Dr. Epstein feels that the current work may help give future research more direction, by pinpointing certain defects in the muscle molecules.

Also, he feels that techniques developed for analyzing the contraction proteins of round worm muscles could be applicable to study of muscle diseases in humans.

Besides muscular dystrophy, the basic research hopes to further scientists' understanding of how the heart muscle works in cardiovascular diseases and diseases of the arteries.

The work is supported in part by the National Institute of Child Health and Human Development.

#

PRESSURE CHECKERS--The National Institutes of Health reports that some dentists and pharmacists are learning how to take blood pressure readings so that they can help Americans learn if they have high blood pressure. The sooner that elevated blood pressure is detected and treated, the better the outlook for the patient.

#

Research Advances

Possible Marker...

HIGH SERUM LYSOZYME MAY HELP DISTINGUISH CROHN'S DISEASE

A Boston scientist has shown that serum concentrations of lysozyme are elevated in patients with Crohn's disease, but not in patients with ulcerative colitis. This suggests that serum lysozyme concentrations might serve as a marker to distinguish Crohn's disease from other inflammatory bowel disorders.

Crohn's disease, or regional enteritis, and ulcerative colitis often overlap in their clinical, radiologic, and morphologic features, creating a problem in diagnosis. The present study was designed to determine if a serum marker might help distinguish Crohn's disease from other forms of inflammatory diseases of the intestine.

Results indicate that serum concentrations of lysozyme, a lysosomal enzyme, are significantly elevated in patients with Crohn's disease, but not in patients with ulcerative colitis or with bacterial or nonbacterial enteritis. The findings suggest that serum lysozyme determinations may be useful in the differential diagnosis of Crohn's disease from other types of bowel inflammation.

Serum lysozyme (muramidase) concentrations were determined in 19 healthy volunteer subjects, in 20 patients with ulcerative colitis, in 25 patients with Crohn's disease, and in six patients with bacterial or nonbacterial enteritis. At least one serum sample was obtained from each of the subjects, who were matched for age, sex, and duration of disease.

The mean serum lysozyme concentration, measured in micrograms per milliliter, was 8.8 in control subjects, 9.3 in ulcerative colitis patients, 26.3

(more)

in Crohn's disease patients, and 8.9 in patients with bacterial or nonbacterial enteritis. The values from patients with Crohn's disease did not overlap those from any other group of patients studied. Thus, mean lysozyme concentrations were significantly greater in patients with Crohn's disease than in patients with other types of bowel inflammation and in healthy control subjects.

No correlation was found between serum lysozyme values and white-cell counts, or between serum lysozyme values and the absolute numbers of circulating granulocytes or monocytes. Elevation of serum lysozyme in Crohn's disease may be a product of tissue macrophages involved in the granulomatous process.

Kurt J. Isselbacher, M.D., of Massachusetts General Hospital and associates reported their findings in the *New England Journal of Medicine*, February 13, 1975. Dr. Isselbacher is a grantee of the National Institute of Arthritis, Metabolism, and Digestive Diseases.

#

RETINAL DISEASES--Diseases of the retina, the light-sensitive tissue at the back of the eye that transmits visual information to the brain, account for more blindness and visual disability in the United States than any other cause, according to the National Institutes of Health.

#

Research Advances

ANTIBODY TREATMENT CAN PREVENT NEONATAL HEPATITIS B INFECTION

Some Denver physicians have reported that prompt specific antibody treatment of infants born to mothers with hepatitis B virus infections prevented chronic neonatal infection. Their work is supported in part by the National Institute of Allergy and infectious Diseases (NIAID).

The University of Colorado Medical Center doctors treated four infants whose mothers' hepatitis B virus infections were determined by the presence of hepatitis B surface antigen (HB_sAg) in their blood. Two of the women had acute infections at or immediately before delivery; the other two had asymptomatic chronic infections. Their infants were treated with specific human antibody to the hepatitis antigen (anti-HB) within two to six days of birth. Regular testing up to the age of 16 months revealed no sign of hepatitis antigen in any of the infants.

The results of a control group of seven mother-baby pairs were quite different. Six of seven untreated babies born to antigen-positive mothers were antigen-positive for five to 36 months. The other baby, born to an asymptomatic HB_sAg carrier, remained antigen free at eight months.

Although serum samples from the placentas of infected mothers are occasionally antigen-positive, there seems to be little correlation with subsequent infection of the infants. The investigators interpret this to mean that HB_sAg is not passed from the mother to the fetus through the placenta, but that the cord blood is sometimes contaminated by maternal blood or secretions. Since antibody treatment does not affect established infection, the excellent results of antibody treatment of these infants also indicates

(more)

that they were not infected in the womb.

The physicians, Peter F. Kohler, Reuben S. Dubois, Deborah A. Merrill, and Watson A. Bowes, of the University of Colorado Medical Center, reported their results in the *New England Journal of Medicine*, December 26, 1974. They suggest that the reservoir of chronic hepatitis B virus infections could be reduced if women were tested at term and the infants of antigen-positive mothers given prophylactic antibody treatment.

#

MIDDLE EAR--Inflammation of the middle ear space can lead to conductive hearing loss by blocking sound which must pass through the middle ear to the inner ear where it is processed and sent to the brain, according to the National Institutes of Health.

ENDOCRINOLOGY--Endocrinology, the study of the internal glandular secretions of the body, is an immense biomedical field which directly pertains to important life functions, such as growth, metabolism, and reproduction, according to the National Institutes of Health.

GLAUCOMA--Glaucoma is an eye disease which strikes one out of every 200 people in the United States over age 40, according to the National Institutes of Health.

#

Research Advances

SCIENTISTS DETERMINE STRUCTURE OF FOLLICLE STIMULATING HORMONE

Two California scientists have determined the chemical structure of human follicle stimulating hormone (FSH), the major component of fertility drugs, an accomplishment which may lead to development of a male contraceptive.

In recent years, investigators have determined the chemical structure of the pituitary gland hormones, thyroid stimulating hormone (TSH) and luteinizing hormone (LH). Investigators at the University of California, Los Angeles, now have determined the amino acid sequence of follicle stimulating hormone (FSH), the only pituitary gland glycoprotein hormone whose structure was still unknown. The finding may lead to development of a male contraceptive.

Previous attemts to determine the structure of FSH were hampered by a lack of human pituitary glands, which are obtainable only at autopsy. The organs used in the present study were provided by the National Pituitary Agency, which is organized and funded by the National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD). With a ready supply of human FSH the investigators, through a series of sophisticated chemical procedures, were able to determine the hormone's chemical structure.

FSH was found to consist of an alpha subunit of 89 amino acid residues, which is identical to the alpha subunit of both LH and TSH, and a beta subunit of 115 amino acids. Surprisingly, the beta subunit of FSH resembles its TSH counterpart more closely than its LH counterpart. The FSH alpha and beta subunits recombined to yield 70 percent of the biopotency of natural FSH.

(more)

Hormone (Cont'd)

The scientists point out that their findings might ultimately lead to the development of a male contraceptive through the immunization of men with anti-FSH globulins that could prevent sperm production that is regulated by FSH. Correction of infertility resulting from inadequate production of FSH in both men and women may also be ultimately achieved through administration of FSH, although synthesis of the large, complex protein is unlikely in the near future.

Albert F. Parlow, M.D., an NIAMDD grantee, and his associate Basudev Shome, M.D., of the University of California, Los Angeles, and the Harbor General Hospital, Torrance, California, reported their study in the *Journal of Clinical Endocrinology and Metabolism,* January 1975.

#

SIDS--The sudden infant death syndrome (SIDS) is the leading cause of death in infants after the first month of life, claiming the lives of three infants for every thousand live births, according to the National Institutes of Health.

FOOD ALLERGIES--The most common food allergies are to fish, berries, nuts, eggs, cereals, milk, pork, chocolate, beans, and various fresh fruits. The National Institutes of Health reports that some people are also allergic to such substances as food additives.

#

Research Advances

SCIENTIST EVALUATES VARIOUS DOSAGES OF CYCLOPHOSPHAMIDE

A Virginia scientist has shown that cyclophosphamide has a dose-related cytotoxic effect on immunoglobulin-bearing lymphocytes in patients with rheumatoid arthritis and systemic lupus erythematosus. This finding might be useful in regulating relatively-safe and effective dosages of this drug.

Grantees of the National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD) reported three years ago that prolonged treatment of severe rheumatoid arthritis (RA) with such immunosuppressive drugs as cyclophosphamide or azathioprine is beneficial--despite the toxicity of these agents--in patients who are refractory to conventional therapy. Guidelines for dosage are still poorly defined, however, and such patients usually receive arbitrary amounts until toxic side effects or clinical improvement (or both) occur.

The present research indicates that cyclophosphamide has a dose-related selective depletion effect on certain immunoglobulin-bearing (B) lymphocytes, and that a reduction of other leukocytes is not necessary for a favorable clinical response. Thus, direct quantitation of B-lymphocytes may aid in regulating clinically effective individual dosages of cyclophosphamide in a relatively safe manner.

Serum samples were obtained from seven patients with RA and four with systemic lupus erythematosus in order to determine baseline counts of small lymphocytes, as well as total leukocytes and lymphocytes. These measurements were repeated after the 11 patients were started on 1.5 to 2.0 milligrams per kilogram cyclophosphamide, and the drug's effects on these cells were

(more)

used to regulate individual dosages of cyclophosphamide.

Small lymphocyte counts which were normal before cyclophosphamide administration, decreased during such therapy. When dosage was reduced to maintenance levels, immunoglobulin-positive small B-lymphocytes were less than 75 percent of normal, while immunoglobulin-negative small T-lymphocytes had returned toward normal. At this time, objective evidence of improvement was observed in 10 of 11 patients.

Adverse side effects of cyclophosphamide, which were rare after 101 total patient months of therapy, included hair thinning, nausea, and two episodes of herpes zoster. Granulocytopenia and marked lymphopenia were not observed, and the data obtained suggest that amounts of cyclophosphamide that produce neither of these severe effects can still be therapeutically effective.

David A. Horwitz, M.D., of the University of Virginia School of Medicine reported his findings in *Arthritis and Rheumatism*, December 1974. His work is funded in part by NIAMDD.

#

POPULATION--The U.S. population has increased 50 percent in the past 30 years and is expected to increase another 50 percent before the year 2000. The impact of population growth cannot be assessed without considering its effects on the health of children, families, and society as a whole, according to the National Institutes of Health.

#

News Feature

At NIH Clinical Center...

NUCLEAR MEDICINE PROVIDES EARLY DIAGNOSIS OF DISEASE

Early and detailed diagnosis is an important factor in effective treatment of some forms of the nation's leading causes of death, such as cancer and heart disease.

The advent of nuclear medicine following World War II provided physicians with a unique way of looking inside the human body, and supplied one of the tools that made early diagnosis possible.

Today, medical tests using radioactive isotopes, or radionuclides, can provide detailed pictures of what is happening in nearly all parts of the body, such as the heart, liver, lungs, kidneys, brain, and blood vessels.

The NIH Clinical Center's Nuclear Medicine Department uses over 12 radionuclides routinely in 27 diagnostic tests. Well over 50 diseases affecting most of the organs and systems of the human body are amenable to surveillance with these techniques. Not only can abnormalities be detected, but progress of disease can be watched and effects of treatment evaluated.

Scientists know that certain chemicals or medicines collect or localize in various parts of the body. In radionuclide tests, a radioactive "tracer" may be administered which localizes in the body part to be studied, or the tracer may be attached to a chemical which will localize in the appropriate organ. With the aid of sensitive electronic devices, the radionuclides can be detected, allowing

(more)

physicians to "see" whether or not the body part or organ is functioning normally. For example, a patient's brain may be visualized by administering a small amount of a radioactive substance, technetium 99m, by vein. A medical radiation detector called a gamma camera is then used to take a picture of the patient's brain.

Radionuclides are promptly eliminated by the body without harm or discomfort. For the most part, the patient receives no more radiation than the minimum exposure from a chest X-ray. Patients need not be hospitalized for most nuclear medical tests, and can return to their homes and families immediately following the studies.

The Nuclear Medicine Department uses several techniques to detect radionuclide activity. One device is the whole body counter, that detects minute amounts of radionuclide and measures the total amount in the body at any one time. The whole body counter is located in a room made of seven-inch thick steel. The room shields the detection equipment as well as the patient from any naturally occurring atmospheric radiation, and thus provides an accurate measurement of radionuclides within the patient. The whole body counter may be used to discern metabolic function. It can be used, for example, to determine a patient's ability to use iron or vitamin B_{12} to form red blood cells. It may also be used to determine the metabolic activity of a variety of cancers.

Another device used in the Nuclear Medicine Department is the scanner or rectilinear scanner. This device has a mobile detector that sweeps back and forth across the patient to trace the distribution of

(more)

radionuclide either in the entire body or in a selected organ. The scanner is not capable of detecting the instantaneous movement of radionuclide within the organ or within a given part of the patient.

A third and most important device, the gamma camera, takes pictures of organs such as the liver or lungs and assesses the blood flow to these organs as well as their size, shape, and function. The flow of radionuclide can be recorded on film, videotape, or computer tape while the radionuclide is being given to the patient who is positioned before the camera. The camera is used to diagnose vascular disorders as well as to detect a variety of diseases in different organs. Unlike the scanner, the gamma camera remains motionless throughout the procedure.

NIH clinicians often ask questions like: Is there cancer in my patient? Where is it located? How widely spread is this cancer? How effective is our new treatment?

The Clinical Center's Nuclear Medicine Department was organized in 1966 to perform radionuclide organ imaging procedures to help answer these questions. For complete answers, it is often necessary to develop entirely new nuclear medical techniques or refine recently developed methods.

As a consequence, the department has devised several unique diagnostic uses for radionuclides. Recent pioneering work with 67 Gallium helped define this radionuclide's usefulness in detecting infections and cancers such as malignant melanoma, histiocytic lymphoma, and Hodgkin's disease that cannot easily be studied otherwise. New Gallium 67 techniques also provide

(more)

a measure for the success of newly developed treatments for cancer by scientists of the National Cancer Institute.

The department is currently developing new diagnostic techniques using a computer coupled to a gamma camera. The computer makes it possible to look at the heart's function and evaluate the efficiency of the heart's pumping action. The nuclear medical method is easier for the patient than cardiac catheterization, and does not require that the patient remain in the hospital.

Scientists in the Nuclear Medicine Department regularly present technical papers at regional and national meetings of professional societies. They also publish research findings in scientific journals.

The physician at the computer (foreground) reads results of nuclear medical tests of a patient in the next room (left with technician). The computer records what happens as the radioisotope passes through a part of the body. The resulting dynamic picture (as opposed to a series of still pictures) permits physicians to watch the entire process. The computer tape can be stored to compare with later scans to observe changes that occur following treatment. (NIH Photo #1372)

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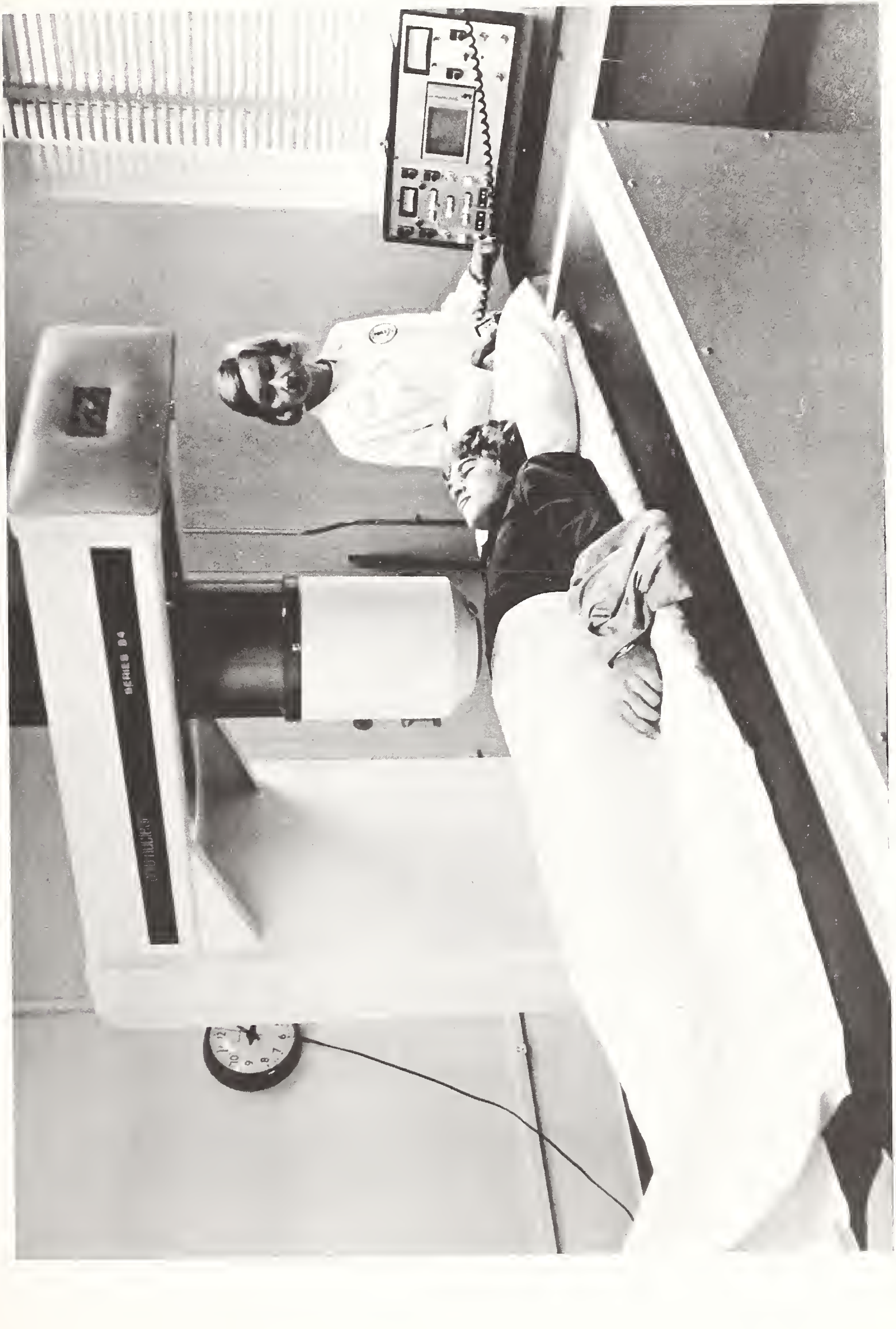
Nuclear Medicine (Cont'd)



This dual probe rectilinear scanner is being used in a total body bone scan. Such nuclear medical tests help physicians determine whether or not a patient has cancer or other abnormalities of the bone. (NIH Photo #1373)

#

News Feature

WARNING: INFANTS GIVEN SUGAR-WATER COULD DEVELOP MASSIVE TOOTH DECAY

Infants given sugar-water or highly sweetened formula in their bottles at bedtime are in danger of developing massive decay of the teeth, warn scientists at the National Caries Program, National Institute of Dental Research. They urge that this practice be condemned by dentists, pediatricians, and others interested in the health of children.

The Dental Institute recently reviewed research findings and clinical reports which reaffirm that sugar is a major factor in causing tooth decay, especially in children and young adults.

According to James P. Carlos, D.D.S., associate director for the Dental Institute's National Caries Program, the scientists further point out: "From the evidence, it is clear that how frequently sugar is eaten is even more important than how much is consumed. Eating sugar-sweetened foods between meals is therefore particularly dangerous to oral health. Children, teenagers, and others who are highly susceptible to decay will develop few cavities if they consistently avoid such snack foods as candies, sweet pastries, and sugar-containing soft drinks, and chewing gums.

"Parents and school authorities are strongly advised to regard these food items as potentially harmful to health and to discourage their use. Sugar-free beverages and chewing gums are available and should be used in preference to their sugar-containing counterparts. Sugar-sweetened foods should be eaten only at regular meals, and only as part of a well-balanced diet."

The scientists conclude that elimination of the habit of between-meals consumption of sugar-containing foods, together with more widespread use of

(more)

fluoride and improvement of oral hygiene, would eliminate tooth decay as a major health problem in the United States.

#

OPEN HOUSE--The first public Open House at the National Institutes of Health (NIH) in more than 20 years is scheduled for April 26 and 27.

As part of HEW's observance of the Nation's Bicentennial, visitors to NIH will be able to see research exhibits, tour laboratories, hear scientist speakers, and view health films between 10 a.m. and 4 p.m. on that Saturday and Sunday.

Exhibits include a working artificial kidney machine, cell separator, typical research animals, germfree animal tank, scientific glassblowing, the life cycle of the wood tick, eyeglasses that simulate the effects of visual diseases, facts about genetic diseases, a whiplash model, and effects of serious injury to the nervous system.

In a series of scheduled lectures for the public, experts will talk about child health, reducing cancer risks, healthy lungs, heart attacks, mental depression, acute leukemia, and diabetes and obesity.

Laboratories and other facilities open for inspection are the NIH Blood Bank, Clinical Center Nuclear Medicine Department, molecular biology labs, computerized patient monitoring systems, and some of the laboratories used by neurological and cancer scientists.

The health films to be shown will cover such topics as understanding the human body, maintaining good health, recent advances in disease research, modern health care techniques, and careers in health professions.

#

Photo Feature

HEATED MITTEN SAVES LIVES OF TRAVELING BABY MONKEYS

A battery-operated heated mitten has been modified to safely transport baby monkeys from the University of Washington's Primate Center field station in Spokane to its Regional Primate Research Center in Seattle.

Prematurely-born or infant monkeys rejected by their mothers are often shipped to the Seattle research facility, which is supported by the NIH Division of Research Resources.

Previously, some of these tiny animals were dying on the 300-mile flight because of the low temperature in the cargo sections of airplanes.

The Lectra-Mit was originally designed by Timely Products Corporation of Fairfield, Connecticut, for hunters and outdoor sportsmen. Gerry Ruppenthal, supervisor of the Center's Infant Primate Research Laboratory, spotted the mitten in a sports store and wondered if it could provide the necessary heat protection for the animals in transport.

The mitten has been modified by Thomas G. Susor, engineering technician of the Instrumentation Development Department, to accommodate the infant non-human primates. Powered by a size "D" Alkaline battery, the Lectra-Mit is capable of generating 180 degrees of heat within five minutes.

Infant pig-tailed macaques, crab-eating macaques, rhesus monkeys, and baboons are fitted snugly into the Lectra-Mit and packed carefully inside a shipping carton for air shipment to the Center where they will receive nursery care. The animals are used for biomedical research and behavioral studies.

The Center reports satisfactory results in the use of the monkey mitten.

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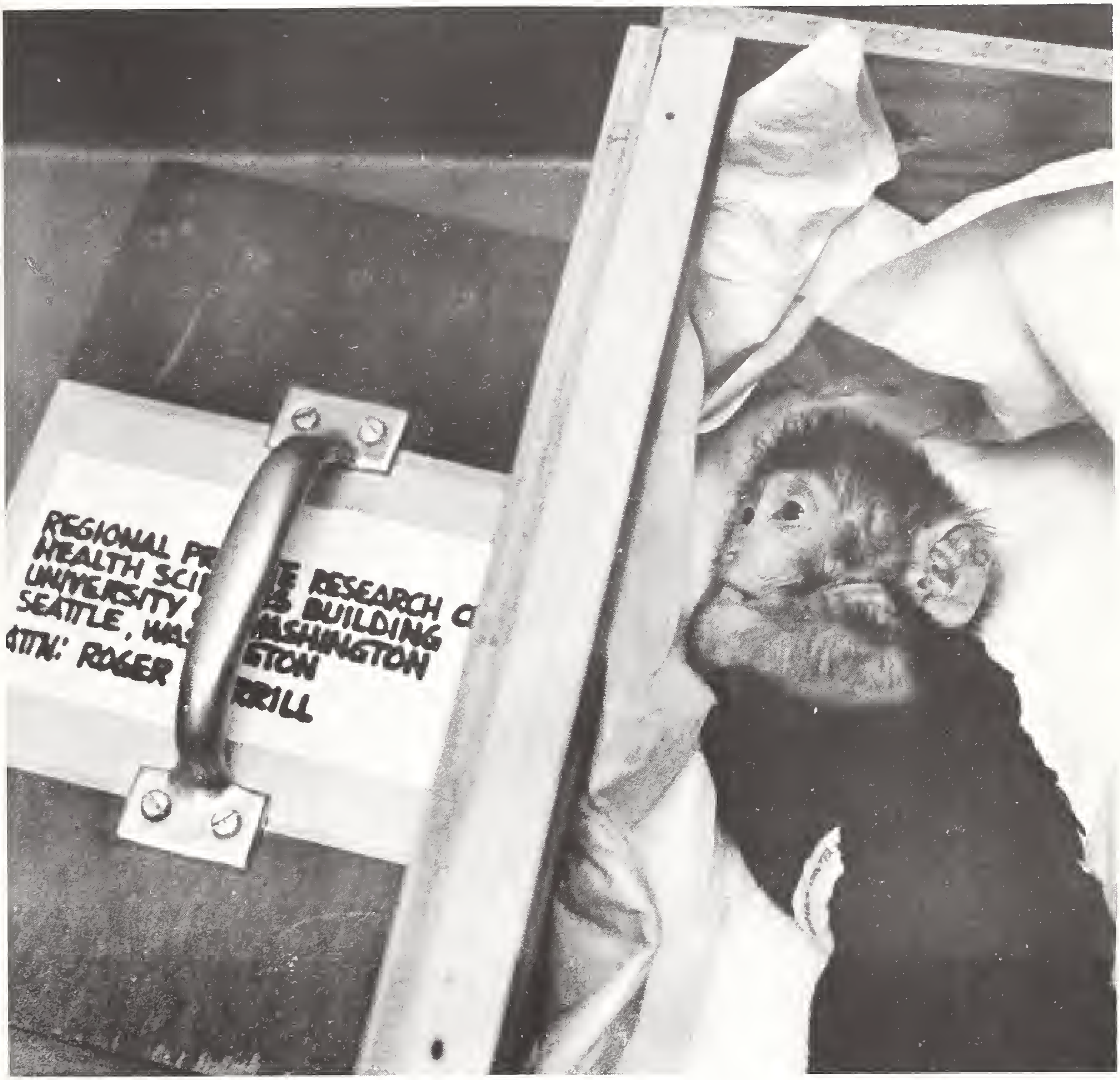

A woolen mitten with self-contained heating unit is being used by the Washington Regional Primate Research Center to transport baby research monkeys in unheated cargo sections of airplanes. Originally designed for the hands of hunters and outdoor sportsmen, the mitten protects the infants during travel. The Center is supported by the NIH Division of Research Resources. (NIH Photo #1374)

#

News Feature

HEART DRUG MAY HELP LIMIT MUSCLE DAMAGE

Nitroglycerin, a drug in use for more than a century to relieve the chest pain of angina pectoris, may also be effective in reducing the extent of heart-muscle damage resulting from acute heart attacks and in reducing the threat of heart-rhythm disturbances that are a frequent, and sometimes lethal consequence of such attacks.

These findings, from a series of studies in animals subjected to coronary artery occlusion, were reported in the January 2, 1975, issue of *The New England Journal of Medicine* by Stephen E. Epstein, M.D., Kenneth M. Kent, M.D., Ph.D., Robert E. Goldstein, M.D., Jeffrey S. Borer, M.D., and David R. Redwood, M.D., of the National Heart and Lung Institute (NHLI) Cardiology Branch.

Most heart attacks result from obstructions in one or more of the coronary branches that supply blood to the heart muscle itself. The heart tissues normally receiving oxygen and essential nutrients via the obstructed vessel may suffer varying degrees of damage, depending upon the severity and duration of blood deprivation (ischemia).

Because the extent and severity of this damage is often a critical factor affecting survival and also the degree of permanent disability following recovery from the acute heart attack, scientists have been seeking effective means of minimizing the destructive consequences of blood deprivation in order to limit loss of functioning heart muscle.

Nitroglycerin had previously been thought unsuitable for this purpose. The drug reduces the oxygen needs of the heart and may also act to improve

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coronary bloodflow by dilating collateral blood channels in heart muscle (both beneficial to the ischemic heart); but it also reduces arterial blood pressure and triggers a reflex increase in heart rate (both of which tend to increase, rather than reduce the area of ischemic heart damage).

In animals subjected to coronary occlusion, Dr. Epstein and co-workers report, nitroglycerin reduced mean arterial pressure by 14 mm of mercury and increased heart rate by an average of 21 beats per minute. But while these factors opposed the beneficial actions of the drug, they did not negate them. The nitroglycerin-treated animals sustained less ischemic heart damage than did the untreated controls.

Moreover, the drop in arterial pressure and increased heart rate usually elicited by nitroglycerin could be prevented by giving the drug in combination with methoxamine, an agent that countered these two effects of nitroglycerin apparently without impeding the drug's beneficial actions in heart muscle.

Nitroglycerin plus methoxamine provided substantially greater protection against ischemic heart damage than had nitroglycerin alone, as indicated by ECG recordings, gross pathological evaluation of affected areas of heart muscle, and biochemical determinations.

In other animal experiments, the investigators found that nitroglycerin also improves the electrical stability of ischemic heart muscle, making the heart less susceptible to dangerous heart-rhythm disturbances, particularly ventricular fibrillation.

The resistance of the heart to fibrillation induced by external electrical shocks was markedly reduced by coronary occlusion, was raised by nitroglycerin, and was restored to near-normal levels by nitroglycerin plus phenylephrine (a

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drug that prevented the fall in arterial pressure normally elicited by nitroglycerin alone).

From these studies, the investigators conclude that, whether by reducing heart oxygen requirements, increasing coronary bloodflow, or both, nitroglycerin helps correct the imbalance between oxygen needs and oxygen availability in blood-deprived areas of heart muscle and thus helps preserve heart tissue that might otherwise be irreversibly damaged by ischemia. In addition, the drug also enhances the electrical stability of ischemic heart muscle and confers some protection against the development of arrhythmias.

In the clinical management of acute heart attacks, nitroglycerin plus methoxamine or phenylephrine may prove valuable in the prevention or treatment of such life-threatening complications as arrhythmias, heart failure, or cardiogenic shock. Such clinical trials are currently in progress at NHLI.

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MONGOLISM--Maternal age is correlated with genetic defects in children. The chances of giving birth to a child with Down's syndrome are five to ten times higher for women over 35, according to the National Institutes of Health.

GOUT--Victims of gout can now be taken care of with reasonable comfort and can be assured that their disorder, if diagnosed early and treated properly, will not cripple them, according to the National Institutes of Health.

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Photo Feature

"JUKEBOXES" HELP STUDENTS KEEP IN TUNE WITH RESEARCH ADVANCES

Irene Petzinger, an audio visual librarian at the Albany Medical College, is shown discussing the selection process of the "medical jukebox" in the College's Schaffer Library of Health Sciences, with Craig A. Emblidge, Class of 1976. The machine, which is the brainchild of the Department of Postgraduate Medicine, is designed to help physicians, nurses, and other health care professionals keep up-to-date with information about current advances in patient care. Several "jukeboxes" are currently in use in community hospitals in northeastern New York. Developmental funds for the "jukebox" project were provided by the National Library of Medicine. (NIH Photo #1375)

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Photo Feature

Separate Programs...

TWO HOUSTON WOMEN RUN NIGMS CENTERS

Two Houston women are among the Center Directors doing important research with NIH funds.

Marjorie G. Horning, Ph.D., is the director of the Center for Research on Toxicological Problems of Drugs, Institute for Lipid Research, Baylor University College of Medicine. This Center is one of 10 supported by the Pharmacology-Toxicology Program, National Institute of General Medical Sciences (NIGMS).

Dr. Horning obtained her Ph.D. from the University of Michigan and spent 10 years with the intramural program of the National Heart and Lung Institute before moving to Baylor University. She is a member of numerous scientific societies and has served on the editorial board of the journal, *Drug Metabolism and Disposition*. She is presently a member of the NIGMS Pharmacology-Toxicology Program Review Committee.

The central theme of the research efforts at Dr. Horning's Center is a combined laboratory and clinical approach to the effects of drugs on the newborn. She and her co-workers have shown that every drug thus far studied, when administered to the mother, undergoes placental transfer, with the result that the fetus and neonate are exposed to a variety of drugs during pregnancy, labor, and delivery. This group has also quantitated the drug exposure which continues after birth, due to breast milk transfer from a mother on chronic drug therapy.

A corollary project at this Center involves study of new pathways of metabolism for drugs. The epoxide-diol pathway, which has been defined

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largely through studies in these laboratories as a pathway for many drugs in common use, has much potential for harm. Epoxides that have been studied have cytotoxic, mutagenic, carcinogenic, or teratogenic properties. The effects of generating a cytotoxic substance in the newborn or in the developing neonate may be far more damaging than similar situations in adults.

In addition to adding to the knowledge base for physicians involved in treating pregnant patients and the newborn, Dr. Horning's Center has become internationally known for its sophisticated technology for the study of drug metabolism. It is one of the nation's most prominent laboratories in the areas of gas chromatography-mass spectrophotometry and computer-instrument interfacing.

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Margery W. Shaw, M.D., is the director of the Center for Medical Genetics and professor of Biology at the University of Texas and the M.D. Anderson Tumor Institute. The Center for Medical Genetics, which includes projects of over 20 investigators, is one of nine supported by the NIGMS Genetics Program.

Dr. Shaw did her undergraduate work at the University of Alabama, received an M.S. in genetics from Cornell University, and received her M.D. degree *cum laude* from the University of Michigan. She is a highly respected investigator in the field of human genetics and cytogenetics and has served on the NIH Genetics Study Section and the NIGMS Genetics Training Committee, the National Science Foundation Genetics Advisory Committee, as well as numerous other committees and organizations. She has been interested in the legal and societal implications of recent developments in human genetics, and has recently completed studies for the L.L.D. at Bates School of Law, University of Houston.

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The Center for Medical Genetics, under Dr. Shaw's direction, includes projects in basic and clinical human genetics, human population genetics, cancer genetics, and legal genetics. The Center contains a clinical genetics unit which provides clinical and laboratory facilities for the diagnosis of genetic diseases as well as research on the attempted treatment of inborn metabolic errors by enzyme replacement therapy. The other studies and projects are concerned with the nature of the germinal and somatic mutations in cancer, and with the genetics of malignancy through the use of human-mouse cell hybrids.

Dr. Shaw has developed a project concerned with questions regarding legal aspects of medical genetics. Among many of the activities of this project is discussion with various organizations on the social, ethical, and legal problems in genetic counseling, genetic screening, and karyotyping.

Shown working in their separate laboratories in Houston are Marjorie G. Horning, Ph.D.,(left), and Margery W. Shaw, M.D. Each woman directs a Center for the National Institute of General Medical Sciences. (NIH Photos #1376, 1377)

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New Publication:
Nurse's Role in Blood Component Transfusion Procurement

The nurse's role in plasmapheresis and other blood component procurement is described in a new publication by the Clinical Center, research hospital of the National Institutes of Health in Bethesda, Maryland.

The publication, *Nurse's Role in Blood Component Transfusion Procurement*, is a monograph of a conference presented to acquaint nurses with the specialized blood collection techniques involved in plasmapheresis, and with nursing care of donors.

The history of plasmapheresis, different methods used to obtain platelets and other components, techniques for working with the equipment, and Hl-A matching of donors and recipients are also discussed.

The conference was presented by members of the Clinical Center Nursing Department who staff the NIH Plasmapheresis Laboratory. To make the conference material available on a wider scale, the edited proceedings are now being published.

Science writers can obtain a free copy of this new publication from: Clinical Center Nursing Department, Building 10, Room 1S-225, National Institutes of Health, Bethesda, Maryland 20014.

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News Releases Issued

HEPATITIS MYSTERY--Many cases of post-transfusion hepatitis may be caused by a yet-to-be identified virus, or viruses, according to National Institutes of Health scientists. Although additional studies are necessary to test this possibility, investigators at the National Institute of Allergy and Infectious Diseases and Clinical Center are the first to obtain serological evidence that some hepatitis occurring after blood transfusions is unrelated to either hepatitis A or hepatitis B--the two forms of the disease most commonly recognized.

MINORITY CONFERENCE--An expanded role for women and members of minority groups in biomedical research supported by Federal funds was the goal of a conference held April 22 to 24 at the National Institutes of Health. Representatives from the faculties and student bodies of approximately 75 minority and women's colleges attended the three-day conference, which was designed to familiarize conferees with activities and research at NIH, and with opportunities for biomedical research support available under NIH grant and award programs. Increased NIH awareness of the resources and capabilities of minority and women's colleges was another result of the conference.

INSTITUTE RENAMED--The National Institute of Neurological Diseases and Stroke (NINDS) has changed its name to the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS). The name change is designed to reflect the Institute's long-standing commitment to improve--through research and training--the diagnosis, treatment, and prevention of diseases which affect

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the ear, nose, and throat. These disorders of hearing, language, and speech affect more than 20 million Americans. The Institute is in the process of a reorganization which will emphasize its major areas of program responsibilities. Its extramural research areas will be divided into four major programs: Communicative Disorders, Neurological Disorders, Stroke and Central Nervous System Trauma, and Fundamental Neurosciences.

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